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ARCHIVES OF SURGERY

VOLUME 15 JULY, 1927 NUMBER 1

ACUTE AND CHRONIC PANCREATITIS

CLINICAL OBSERVATIONS

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PART I

The diagnosis of many pancreatic conditions is so difficult that a large proportion of the cases reported in the literature were definitely diagnosed only at operation or autopsy. Hence it is certain that the incidence of these conditions is probably far greater than has been generally recognized. The difficulty in diagnosis is largely due to three facts: 1. The pancreas is so deeply situated that it is usually inaccessible to palpation. 2. It is impossible to obtain a secretion from it in a state sufficiently pure for purposes of examination. 3. These diseases are often associated with other disorders of the digestive tract the symptoms of which are so prominent that they mask those produced by the pancreatic lesion.

It is our purpose in this communication to report briefly some of the cases of acute and chronic pancreatitis which have come under our observation. The following were cases of acute pancreatitis:

CASE 1.—*Acute pancreatitis in a diabetic patient with gallstones and acute nephritis. Drainage of gallbladder followed by death within a few hours.*

M. M., a woman, aged 67, was admitted to the Hebrew Hospital on April 22, 1917. She had suffered from a mild type of diabetes for a number of years, but otherwise had had exceptionally good health. The acute illness was of less than twenty-four hours' duration. She was suddenly attacked with pain in the umbilical region, which traveled in the direction of the gallbladder and down toward the appendix. For six hours before admission there had been almost continuous vomiting of coffe-ground-like material. The bowels had been constipated for some time.

When first examined the patient was in a state of shock. The temperature was subnormal, the pulse was rapid, and the extremities were cold. The abdomen was distended, and there was marked rigidity with extreme tenderness

in the epigastric area. The leukocyte count was 26,000. The urine contained albumin, a few red cells and many hyaline and granular casts.

The diagnosis of intestinal obstruction was made, although the possibility of acute pancreatitis was considered. An operation was performed at once. The abdomen was opened through a right rectus incision, and about a quart of free wine-colored fluid was found in the abdominal cavity. The gallbladder appeared distended, and the adipose tissue was covered with small white dots. These measured 1 mm. or a little more in diameter, and were perfectly flat. At first they looked much like miliary tubercles, but on closer observation were recognized as areas of fat necrosis. In the region of the pancreas and the gallbladder there was considerable subperitoneal edema. We were undoubtedly dealing with acute pancreatitis. The gallbladder was drained; it contained a moderate amount of dark bile and a few small stones, hardly more than 1 mm. in diameter.

Following the operation the patient continued in a state of shock, and the outlook appeared most unfavorable. She rallied again, however, but relapsed and died in a few hours.

CASE 2.—*Acute pancreatitis; gallstones; drainage of gallbladder. Recovery.*

J. B. E., a woman, aged 24, was admitted to the Church Home and Infirmary on March 31, 1919, complaining of intense abdominal pain. She had enjoyed good health and normal digestion until nine months before, when she had become pregnant. On various occasions during this period she had been seized with acute abdominal pain, located under the right costal arch and extending toward the right shoulder-blade. She had not had chills or fever, but on at least one occasion the attack had been followed by jaundice. There was constant tenderness under the right costal arch. In addition the patient was frequently troubled with eructations of gas and pain in the epigastrium which were relieved by the use of soda. A diagnosis of cholelithiasis had been made. The patient had gone through a normal confinement two weeks prior to entering the hospital, and during the two or three days before had had several attacks of pain in the region of the gallbladder, associated with fever. Hypodermic injections of morphine had been necessary. Later the pain radiated from the midepigastrium to the left side and the back, and considerable quantities of a yellowish fluid had been vomited; there was obstinate constipation. On examination, the patient appeared to be in a state of shock. The pulse was rapid, the temperature was subnormal and the extremities were somewhat cold. The abdomen was slightly distended. There was rigidity and extreme tenderness over the entire epigastric area. The urine contained a slight trace of sugar, albumin and acetone, and microscopic examination showed leukocytes, red blood cells and epithelial cells.

A diagnosis of cholelithiasis with possible perforation was made, and immediate operation was advised. A right rectus incision was made, and a yellow serous fluid was at once encountered. Milky patches of fat necrosis were noted in the omentum and peritoneum. These varied from 1 to 3 mm. in diameter, and were evidenty caused by acute pancreatitis. There was marked subperitoneal edema, especially in the region of the pancreas. The gallbladder was free from adhesions. It was not enlarged, but contained about thirty to forty small mulberry-like stones, varying from 1 to 2 mm. in diameter. The bile was inky black and thick. The mucosa of the gallbladder was red, vascular and granular. A few of the small stones passed into the gallbladder from the

cystic duct. A rubber drainage tube was inserted into the gallbladder, and three cigaret drains were placed around it. The patient made a satisfactory recovery, and was discharged well on April 17, 1919.

CASE 3.—*Acute pancreatitis in a patient with cholelithiasis. Drainage of gallbladder. Recovery.*

E. R., a woman, aged 60, was admitted to the Church Home and Infirmary on April 9, 1925. She had always been in good health except for attacks of indigestion following meals, which had occurred at irregular intervals for some years. They were characterized by the presence of pain, gas, eructations, and occasionally nausea and vomiting. The attacks were of short duration; there were marked constipation and melena or clay-colored stools; jaundice was absent.

On the evening of April 7, 1925, the patient was suddenly seized with violent epigastric pain, nausea and vomiting necessitating the use of morphine. There was intense pain in the epigastrium above the umbilicus and under the left costal arch, associated with intense nausea and frequent vomiting of a biliary secretion.

When she was admitted to the hospital two days later, she looked ill and was in a state of shock; the extremities were somewhat cold; the pulse was rapid, and she was extremely thirsty. She appeared to be in great pain, and was unable to sit up or turn over.

Deep inspiration caused pain in the upper right quadrant. The abdomen moved but slightly in inspiration; the walls, however, were not rigid. There was tenderness under the right costal arch and in the epigastrium. There was a leukocytosis of 22,700. The urine was normal except for a trace of albumin.

The conclusion was that we were dealing either with an acute cholecystitis associated with a possible acute pancreatitis, or perhaps with a perforating peptic ulcer.

The abdomen was opened through a McBurney incision. A turbid fluid containing small flakes escaped when the peritoneum was incised. The appendix was removed and proved to be two and a half times its normal size and enlarged toward the tip. An upper right incision was then made, and the gallbladder was exposed. It was tense and slightly adherent. As the omentum between the stomach and transverse colon was drawn up, a white spot, about 1 mm. in diameter, was noted, and when more of the omentum was exposed, it was found to contain many small areas of fat necrosis. With the brilliant yellow fat and striking white patches, the picture of fat necrosis, pathognomonic of an acute pancreatitis, appeared definite. The gallbladder was drained, and several small stones, together with a conglomerate calculus 1.5 cm. in diameter, were removed. A rubber drainage tube was inserted into the gallbladder, and two cigaret drains laid beneath it. Marked subperitoneal edema was noted around the pancreatic region. The pelvis was drained through the appendix incision. The operation was followed by severe nausea and vomiting for a few days, and the incisions were slow in healing. The patient was discharged, however, on May 10, 1925, in good condition.

CASE 4.—*Acute pancreatitis with gallstones and subsequent abscess formation. Recovery.*

V. B., a woman, aged 34, first consulted us on Feb. 18, 1925. She had had good health until three months before, but since then had complained of gnawing pains of a mild type in the upper part of the abdomen occurring at irregular intervals. For the past month she had been seized once or twice weekly with

violent pains under the costal arch radiating into the right side of the back and frequently toward the right shoulder-blade. These attacks were of about two hours' duration, and necessitated the use of morphine hypodermically. During the attacks there was much distention and gaseous eructation. Fever and jaundice were not noted.

On examination the edge of the liver was palpable, but tenderness could not be elicited. The urine was normal; the gastric contents following an Ewald

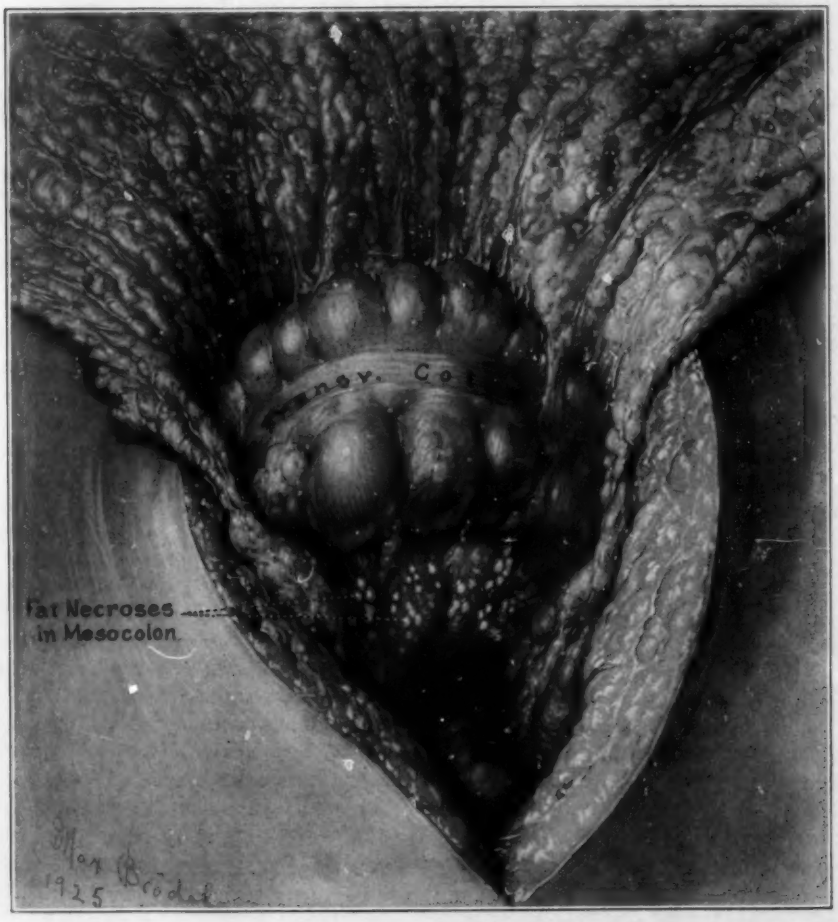

Fig. 1.—Fat necroses in the omentum.

test breakfast showed: total acidity 26, free hydrochloric acid, 19. A gastrointestinal roentgen-ray series showed adhesions in the upper right quadrant, but no radiable stones. Cholecystitis with possible cholelithiasis was diagnosed.

The patient continued to have occasional attacks of a similar type until Sept. 18, 1926. After that time she had three severe attacks of pain. During the last attack a new feature developed, in that the pain, which had previously

been localized, became general and was accompanied by tenderness over the entire abdomen.

The patient was admitted to the Johns Hopkins Hospital on Sept. 25, 1925. Examination revealed: normal temperature; pulse rate, 78; hemoglobin, 78 per cent; leukocytes, 15,480. She complained of considerable generalized abdominal pain and discomfort. She was slightly jaundiced, and there was an extreme tenderness over the gallbladder region, and generalized sensitiveness over the entire abdomen. Muscle spasm or rigidity was not present, nor was there evidence of free fluid in the abdomen. The urine contained bile, but was otherwise normal.

Fig. 2.—Fat necroses in the mesentery of the transverse colon.

A diagnosis of cholelithiasis with possible acute pancreatitis was made. When the abdomen was opened, small, flat whitish yellow areas, about 1 mm. in diameter or smaller, were found scattered over the surface of the omentum (fig. 1). In the omentum between the stomach and transverse colon there was an area, about 2 cm. in diameter, sharply circumscribed, somewhat puckered, and containing myriads of these little areas of fat necrosis. The omentum and transverse colon were then pulled up, and where the mesocolon lay over it a greatly enlarged pancreas could be detected. The organ was fully four times its natural size, and the fat presented numerous small areas of necrosis (fig. 2). There were also stringy grayish blue areas in the fat, suggesting that abscesses

might be developing. Adhesions did not appear between the peritoneum of the mesocolon and that adjacent to it.

The gallbladder was incised, and three stones, each about 1 cm. in diameter, were removed. The stones were composed of smaller ones which had fused. There were also a number of small stones. Examination of the cystic and common ducts failed to reveal any further calculi. The gallbladder was drained with a rubber tube; three drains were placed around it, and another was carried down in the foramen of Winslow. Following the operation the patient was in a state of extreme shock, and the outlook was not particularly good.

Cultures taken from the gallbladder and peritoneal cavity were all negative. After operation, the temperature was normal; the incision healed *per primam.* The gallbladder tube was removed on the fourteenth day. The patient's appetite was very poor during the first two weeks, and during the third week she vomited continuously. The temperature began to rise, and during the third week it went as high as 101.5 F. She lost ground, could not retain any food, became weak and drained bile profusely through the fistula. On the twenty-first day a definite mass, occupying the lower third of the gallbladder incision, could be palpated. This mass appeared to be about 9 cm. in diameter.

On Oct. 19, 1925, a small incision was made over the lower third of the previous one, and induration in the fat was encountered. The indurated area was carefully penetrated with Kelly forceps, and fetid pus was found at once. After this had been carefully wiped off, long strings of what appeared to be disintegrated fat were removed. Some of these strings were fully 3 cm. long and 1 cm. broad. The wall of the abscess cavity was carefully palpated, and seemed to be intact at every point. The cavity was loosely packed with plain gauze. From the pus *B. coli* was grown in pure culture. The patient returned to the ward in splendid condition, and her convalescence from that time was uninterrupted. The drains were removed by the seventh day, and the temperature became normal on the eighth day. The bile escaping from the gallbladder fistula decreased just as soon as the abdominal abscess was opened. The fistula closed completely on the seventh day after the second operation.

The patient lost 18 pounds (8.2 Kg.) during her stay in the hospital. When she left she had a splendid color, a good appetite, and was feeling well. The abscess incision was closing rapidly, but had not completely healed. She was discharged from the hospital on Nov. 1, 1925. Microscopic examination of the necrotic tisue removed revealed that it consisted largely of necrotic fat.

ACUTE PANCREATITIS

Acute pancreatitis, according to the classical publication of Fitz,[1] occurs in three forms: hemorrhagic, gangrenous and suppurative. These three really represent various stages of the same process, which starts as an acute hemorrhagic lesion. It was Fitz, too, who first pointed out the clinical importance of fat necrosis and its relation to hemorrhagic and

1. Fitz: New York M. Rec. **1**:197, 225 and 253, 1889; Boston M. & S. J. **127**:571, 1892.

gangrenous pancreatitis, although this condition had been previously alluded to by Balser [2] and by Chiari.[3]

In establishing the etiology of the hemorrhagic variety, it has been a question, according to Oser,[4] whether the hemorrhage is primary and the inflammatory condition secondary or vice versa. According to Opie,[5] inflammation is not present at the onset, and he therefore prefers the term hemorrhagic necrosis to that of hemorrhagic pancreatitis.

The gangrenous form is a later stage of the hemorrhagic lesion, while the suppurative variety is characterized by the formation of single or multiple abscesses.

ACUTE HEMORRHAGIC PANCREATITIS

This condition has also been termed pancreatic hemorrhage or acute hemorrhagic necrosis of the pancreas, for in it hemorrhage has been noted as a primary manifestation, followed subsequently by an inflammatory process. As we have already pointed out, in those instances in which hemorrhage and inflammatory changes are both present, it is usually impossible to decide which is the primary condition.

Opie [6] has pointed out that the passage of bile into the pancreatic duct produced by gallstones in the diverticulum of Vater is a cause of hemorrhagic necrosis, and Archibald [7] has shown that in addition, an infection of the bile is necessary in order to bring about this result. In most of the instances reported cholelithiasis was observed. According to Egdahl,[8] in 42 per cent of these cases calculi are present either in the diverticulum of Vater or at the duodenal orifice of the pancreatic duct, and Opie considers this percentage too low. Gallstones were present in all four cases in our series.

Eggers [9] maintains, from a study of his own cases, that infection is of minor importance as a causative factor in acute pancreatitis, but that the condition is brought about by the action of liberated pancreatic ferments on the surrounding tissues, in addition to some inflammatory condition associated with the gallbladder.

On the other hand, Ballantine [10] considers that trauma plays an important rôle, and that common duct obstruction as well as infectious

2. Balser: Virchows Arch. f. path. Anat. **90**:520, 1882.
3. Chiari: Prag. med. Wchnschr. **30**:285, 1883.
4. Oser, in Nothnagel: Diseases of the Pancreas, Philadelphia, W. B. Saunders Company, 1903, p. 117.
5. Opie, in Osler: Modern Medicine, ed. 3, Philadelphia, Lea & Febiger, 1926, vol. 3, p. 669.
6. Opie: Bull. Johns Hopkins Hosp. **19**:182, 1901.
7. Archibald: Surg. Gynec. Obst. **28**:529 (June) 1919.
8. Egdahl: J. Exper. Med. **9**:385, 1907.
9. Eggers: Ann. Surg. **80**:193, 1924.
10. Ballantine: J. Oklahoma M. A. **27**:264, 1924.

diseases predispose to this condition. Cases in which trauma was noted as a cause of acute hemorrhagic necrosis, for instance, from a blow on the abdomen, have been reported by Selberg [11] and others.

Hofer [12] is of the opinion that, while biliary disease plays a most important rôle in the etiology of acute pancreatitis, inflammation can also be transmitted through the lymphatics, and that the changes occurring in the pancreas are attributable to the presence of trypsin-infected bile or duodenal contents. Marked inflammatory disturbances of the duodenum, with a consequent ascending infection, have also been thought responsible for this condition.

McCrae [13] says that cases of acute pancreatitis have been observed at autopsies after death from infectious diseases. He believes that in these cases attacks of acute pancreatitis are present, but are so mild that they are frequently not recognized—a fact that would suggest a probable etiology by a hematogenous route.

Acute hemorrhagic pancreatitis occurs most frequently in men, although the four patients of our series were all women, the ages ranging between 24 and 67. The autopsy observations vary according to the duration of the lesion. The omentum and mesentery, retroperitoneal fat and abdominal peritoneum present a large number of yellowish white areas of fat necrosis varying in size from that of a pea to that of a dime. There is also often free blood-stained fluid in the lesser peritoneal cavity. It is not unusual to find gallstones and dark grumous bile in the gallbladder, and occasionally gallstones may be palpated in the common duct or in the ampulla of Vater. The pancreas is usually enlarged and firm, dark, or mottled and friable. Many areas of fat necrosis are observed on the surface. The hemorrhagic necrosis spreads deeply downward, involving areas of both parenchyma and interstitial tissue, but leaving intermediate spaces of normal tissue. The cells of the parenchyma involved are in a state of necrosis with complete loss of nuclei. The necrosis also implicates the blood vessels of the pancreas, and produces hemorrhages of a more or less marked degree. Colon bacilli and streptococci are the usual organisms present.

Symptoms.—Acute hemorrhagic pancreatitis frequently occurs in persons who have suffered from previous attacks of indigestion or biliary colic with or without jaundice. In these attacks, in addition to the pain, which may be of the biliary colic type or suggest gastric or duodenal ulcer, in some instances there is also nausea and vomiting. Ordinarily the attack begins with a sudden and violent pain, which is referred to the epigastrium and in some instances extends to the back or

11. Selberg: Berl. Klin. **38**:923, 1901.
12. Hofer: Arch. f. klin. Chir. **131**:313, 1924.
13. McCrae: Atlantic M. J. **28**:555, 1925.

loins. It may occur in intermittent paroxysms, but is usually constant. In acute cases it may continue until death, which may occur even within a few hours. The pain may be so violent as to suggest rupture of a peptic ulcer or of the gallbladder. Collapse is common, with the usual symptoms of shock, a rapid, faint pulse, low blood pressure and cold extremities. Nausea, vomiting and hiccup are early manifestations, and constipation is usually so obstinate as to suggest an acute intestinal obstruction. In other instances diarrhea is an early symptom and ordinarily follows constipation, if this condition has previously been present. In rare instances jaundice occurs. Fever is rarely noted, though a leukocytosis is common, and glycosuria is occasionally found. In a case reported by Rodriguez,[14] an acute pancreatitis was associated with glycosuria, and the patient died in a diabetic coma. Dunn [15] observed two cases in which diabetes followed as a sequel. In case 1 of our series, the patient had a mild diabetes, and was suddenly taken with violent pain in the umbilical region, which was accompanied by continuous vomiting and signs of shock. The constipation was so obstinate that a diagnosis of intestinal obstruction was made.

In case 2 there had been definite evidence of former biliary colic with jaundice. Pain was extreme in the epigastrium and radiated toward the left side. Vomiting and marked constipation were present.

In case 3 the patient had had indigestion for years. It culminated in a sudden attack of violent epigastric pain, which radiated toward the left side and was followed by nausea, vomiting and shock.

In case 4 there was a definite history of gallstone colic followed by an attack of general abdominal pain and jaundice.

Examination in these cases reveals extreme tenderness in the epigastrium above the umbilicus, not only in the midline, but spreading across the abdomen to both sides. In the early stages there is an absence of rigidity in this area, but soon this sign becomes marked. An indistinct resistance may often be noted at first in this region on deep palpation, but as a rule, a tumor mass is rarely palpable until after three or four days. Slate-colored patches are often observed on the abdomen and limbs, a condition which is associated with lividity of the face. These are certainly rare in other acute abdominal disturbances.

In cases 1 and 2 of our series there was extreme tenderness and rigidity in the epigastrium, while in case 3 there was tenderness under the right costal arch and also in the epigastrium. In case 4 there was marked tenderness over the gallbladder region with a general sensitiveness over the entire abdomen.

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14. Rodriguez, Juan: Acute Pancreatitis with Fat Necrosis, Complicated by Diabetic Coma, J. A. M. A. **82**:203 (Jan. 19) 1924.

15. Dunn: Lancet: **1**:595 (March 20) 1926.

Death may occur within a few hours or days; but if the patient survives for a period of a week or two, the stage of gangrenous pancreatitis ordinarily supervenes.

In addition to the fulminating types of acute hemorrhagic pancreatitis, there are milder forms in which recovery occasionally takes place. Instances of this form have been reported by Waring and Griffiths.[16] Pain of any marked degree was observed in only about half of their cases. Brocq[17] also points out that hemorrhagic pancreatitis is sometimes a mild condition in which pain is more or less diffuse, and is most severe at the end of digestion.

ACUTE GANGRENOUS PANCREATITIS

This condition usually follows the hemorrhagic form, in which the symptoms manifested have been of a milder or subacute type. The pancreas presents a soft, friable appearance, and is darkish with yellowish areas of necrosis, which may be extensive. The lesser peritoneal cavity may be partly filled with necrotic, sanguineous, putrid contents. There is an extensive fat necrosis present around the pancreas and in the lesser peritoneal cavity, in which infections are caused by various forms of micro-organisms. General peritonitis is rarely produced, as the adhesions prevent the escape of infected fluid into the peritoneal cavity. Histologically, the boundaries between the acini of the pancreas become indistinct, and are replaced by granular detritus intermingled with red blood cells, the walls of the capillaries undergoing fatty degeneration.

Symptoms.—If death does not occur as a result of the hemorrhagic stage, manifestations of gangrenous pancreatitis supervene. The fulminating symptoms now subside. The pain, tenderness and vomiting lessen, and the constipation is relieved. Recurrences of a milder type, however, are not infrequent.

The onset is characterized by fever and the formation of a mass in the epigastrium within a week or two after the beginning of the hemorrhagic stage. It may begin with a chill, or chills may occur during the course of the fever. The temperature is usually irregular, ranging from 100 to 103 F. or higher. Only rarely is fever absent; a leukocytosis is the rule. The tumor in the epigastrium is ordinarily fairly definite, though it may vary in size, at times extending as far to the left as the spleen. At this stage the stools become soft, not infrequently diarrheic, and jaundice may occur. Glycosuria is unusual, though cases of diabetes following this condition after several months have been reported.

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16. Waring and Griffiths: Brit. J. Surg. **11**:476, 1924.
17. Brocq: J. de chir. **25**:7, 1925.

ACUTE SUPPURATIVE PANCREATITIS

Acute suppurative pancreatitis frequently follows hemorrhagic or gangrenous pancreatitis. In this form bacterial invasion is common, so that suppuration with abscess formation is frequent. In some instances acute suppurative pancreatitis occurs as a primary infection. The purulent inflammation may extend to the lesser peritoneal cavity and produce peripancreatic abscesses. The infection may occur as a result of extension from adjacent organs through the blood stream, but it most commonly originates in the ducts. Many cases are caused by obstruction of the duct of Wirsung, due to the presence of gallstones in the diverticulum of Vater. In some instances a suppurative cholangitis has been noted as a causative factor.

Small multiple abscesses are present throughout the entire pancreas or are limited to certain areas. Large foci are produced by the coalescence of small abscesses, and as a result parts of the gland are destroyed.

Symptoms.—The nature of the onset depends largely on its cause; that is, whether the condition is a result of an antecedent acute hemorrhagic or gangrenous pancreatitis or is due to carcinoma or suppurative inflammation of the bile passages. In most instances acute suppurative pancreatitis comes on suddenly, following an attack of indigestion or biliary colic, with severe epigastric pain, which may radiate throughout the abdomen. There is epigastric tenderness. Nausea and vomiting are early manifestations. Fever of an irregular type is present, and chills are not uncommon. Constipation is usual and at times is followed by attacks of colliquative diarrhea. Abscesses occasionally rupture into the intestine, and blood and pus are discharged in the stools. Jaundice is common, and leukocytosis is often observed. Glycosuria is rarely noted.

In some instances the symptoms are of a milder type, the onset being less stormy and the pain less intense. In such cases there is often more discomfort without fever but with anorexia and weakness. The pains and fever gradually subside, and the disease may then pursue a more or less chronic course with periods of exacerbation.

Physical examination shows that the liver and spleen are enlarged; the epigastrium is distended, and in a certain proportion of instances a tumor mass or definite resistance can be felt on palpation. Case 4 of our series represents our only case of acute suppurative pancreatitis. The patient, three weeks after an operation for acute hemorrhagic pancreatitis, began to manifest signs of the suppurative form. The appetite became poor, and she began to vomit continuously; her temperature rose to 101.5 F., and bile drained profusely from the fistula. A mass was then detected.

The extension of the inflammation brings about a peritonitis as a complication of acute suppurative pancreatitis. This usually occurs in

the encysted form, and is limited to the lesser peritoneum, though in some instances general peritonitis develops.

Diagnosis.—The sudden and fulminating onset of pain in the epigastrium accompanied by symptoms of shock points directly to the presence of acute hemorrhagic pancreatitis. The principal conditions from which it has to be differentiated are acute intestinal obstruction, especially if obstipation is present, cholelithiasis with rupture of the gallbladder, perforation of a peptic ulcer and mesenteric thrombosis.

When the transition from the hemorrhagic to the gangrenous type occurs, the epigastrium becomes distended, and a tumor mass becomes palpable in the epigastrium. Chills and fever are the rule.

As suppurative pancreatitis frequently follows the hemorrhagic and gangrenous forms, the history may sometimes furnish important information to help in the diagnosis. When a mass in the region of the pancreas occurs with chills and fever, suppuration must be suspected. If an abscess of this type ruptures into the intestine, the character of the stool serves as an aid in diagnosis. It is usually impossible to differentiate between the gangrenous and suppurative types.

The laboratory examinations are of distinct aid at times in the diagnosis of acute pancreatitis. The presence of glycosuria is especially valuable, and Musser [18] has pointed out the importance of a high sugar content in the blood in these cases.

Course and Prognosis.—In the fulminating types with hemorrhage, death frequently occurs within a few hours or days. Many surgeons, among them Moynihan,[19] Vogel [20] and Ansperger,[21] advise operation as a routine. On the other hand, the operative risk in the acute cases is so great that, if possible, according to our own experience, it is best to delay surgical intervention until the shock has somewhat subsided. When the disease has progressed to the gangrenous and suppurative stages, operation is indicated, but in these cases it often fails to save the patient, owing to the extent of the lesion and the multiple abscesses which have formed. However, whenever a large single accumulation of pus within the pancreas can be evacuated by incision and drainage, recovery may be expected.

Treatment.—As has already been pointed out, except in rare instances little can be hoped for from surgical measures in the acute fulminating types of hemorrhagic pancreatitis. For immediate relief in allaying the violent pain and lessening shock, morphine in adequate doses is indicated; sometimes inhalations of chloroform may be utilized.

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18. Musser: New Orleans M. & S. J. **78**:10 (April) 1926.
19. Moynihan: Ann. Surg. **81**:132, 1925.
20. Vogel: Deutsche Ztschr. f. Chir. **185**:71, 1924.
21. Ansperger: Deutsche Ztschr. f. Chir. **189**:189, 1924.

Vomiting may often be controlled by means of gastric lavage and by the avoidance of food by mouth. The strength is best maintained with glucose by proctoclysis, and in addition normal salt and soda solution. Subcutaneous and intravenous injection of normal salt or glucose solution should be employed.

Statistics supplied by Gessner [22] indicate that operations performed during this stage are more often fatal than during the later stages, that is, in the gangrenous and suppurative types. According to his data of forty-one cases of this disease in which an operation was resorted to during the first two weeks, recovery occurred in but one case (Halsted's), whereas of the twenty patients operated on during the later stages six recovered. Mayo-Robson and Cammidge [23] attribute the high mortality from early operation in acute cases to the fact that in many of these fatal cases intestinal obstruction had been suspected, and that these patients, already in a state of shock, were subjected to a prolonged search for the suspected lesion. Of fifty-nine of their patients operated on during the acute stage, twenty-three recovered (39 per cent).

Operation, however, is always indicated during the gangrenous and suppurative stages, and should be performed without delay. As has already been indicated, if the abscess is single and localized, recovery may be expected as a result of effective drainage.

When operation has been decided on, an upper median abdominal incision should be made, and, as advised by Moynihan,[19] the pancreas should be approached through the gastrohepatic omentum, gastrocolic omentum, or in rare instances through the transverse mesocolon after reflection of the omentum. The pancreas should be cautiously isolated, packs being utilized with meticulous care in order to prevent the escape of the toxic pancreatic fluid into the peritoneal cavity. Evacuation of pancreatic fluid (if large quantities are present) is accomplished by aspiration, followed by incision into the pancreatic capsule and superficially into the gland itself to release fluid, blood and pus. Finally, thorough drainage should be obtained by means of gauze surrounding a drainage tube passing through the anterior abdominal wall. Posterior drainage, in addition, is sometimes necessary. If the condition of the patient admits, gallstones, if present, should be removed.

The discovery of fat necroses at operation confirms the diagnosis. According to Mayo-Robson and Cammidge, of six patients operated on for abscess of the pancreas, recovery occurred in five (80 per cent), although in one instance relief was afforded only for a few weeks and in another but for a few months.

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22. Gessner: Deutsche Ztschr. f. Chir. **54**:65, 1899-1900.

23. Mayo-Robson and Cammidge: The Pancreas, Its Surgery and Pathology, Philadelphia, W. B. Saunders Company, 1907, pp. 404, 409 and 433.

PART II

CHRONIC PANCREATITIS

For the reasons already given, the incidence of pancreatitis is far higher than is generally recognized. However, as a result of more careful study of the clinical manifestations, together with the results obtained through the laboratory observations, especially from the examination of the duodenal contents for pancreatic ferments, the diagnosis can now be made in many cases which heretofore would have been detected only at operation or autopsy.

Brief abstracts of the histories of fifteen cases of chronic pancreatitis studies are given below.

CASE 1.—*Indefinite but urgent abdominal signs. Unusual twisting of the duodenum, chronic pancreatitis.*

Mrs. D. H. T., aged 40, for eight months had had marked indigestion, pain and a feeling of pressure after meals, nausea and occasional vomiting. She had had frequent diarrhea, had lost much flesh and complained of extreme weakness. On March 12, 1903, she was suddenly seized with violent abdominal pain which was followed by intense shock. When she was first seen, her appearance strongly suggested an abdominal perforation. There was a definite board-like rigidity over the entire right side of the abdomen. The patient had a subnormal temperature and rapid pulse and was extremely ill. Further examination could not be made. An exploratory incision at the Cambridge Hospital revealed a twisted and somewhat thickened duodenum. The pancreas was much enlarged and extremely hard and thickened. Fat necrosis, however, was not noted. The duodenum was straightened out as far as possible. The patient, although in a state of extreme shock during the entire operation, soon improved and made a rapid recovery.

The pancreas, though presenting the typical appearance of a chronic inflammatory condition, could hardly have accounted for the acute symptoms, which were in all probability produced by a sudden twist in the duodenum.

CASE 2.—*Chronic pancreatitis with symptoms suggesting cholelithiasis or cancer.*

J. C. D., aged 35, first consulted us on March 27, 1903. For the preceding five or six years the patient had had digestive disturbances, being unable to eat certain articles of food. He was easily nauseated by disagreeable sights and odors, and for fourteen years he had had occasional attacks of abdominal colic.

About August, 1902, he began to suffer pains in the right lumbar and hypochondriac regions. These were not constant and were varied in severity; at times they were sharp and lancinating, at other times dull and aching. The patient had complained of indigestion, which had been more or less acute during this period. These attacks were characterized by severe nausea and frequent vomiting, which would appear suddenly, most frequently at night, accompanied by severe pains in the epigastrium. The vomited material consisted mainly of undigested food particles and mucus; occasionally it contained blood. There was often a gushing of saliva into the mouth. After the severe pain disappeared, a soreness would still remain over the abdomen. The fulminating pains and attacks of vomiting, which occurred only occasionally at first, became more frequent, so that he had attacks every three or four days. The

bowel movements were diarrheic, and occasionally contained blood, especially after a severe attack. The patient had lost 40 pounds (18.1 Kg.) in weight.

On examination he was found to be emaciated. The mucous membranes were pale, his face was much drawn, his tongue slightly coated; the pulse was weak, the radial arteries were slightly thickened, and the heart and lungs were normal.

The abdomen was somewhat distended; the surface presented a distinct cyanotic appearance, and the capillaries were markedly distended. There was tenderness in the epigastrium and beneath the right costal arch. The gastric contents after an Ewald test breakfast showed: total acidity, 40; free hydrochloric acid, 0; much mucus. The urine was normal. A blood count showed: red blood cells, 5,168,000; leukocytes, 5,625; hemoglobin 50 per cent. Otherwise the patient was normal. At first the case was considered one of cholelithiasis; on the other hand, the rapid emaciation, together with the absence of free hydrochloric acid in the gastric contents, pointed in a measure to carcinoma of the stomach, notwithstanding the absence of palpable tumor. The diagnosis appeared so doubtful that the patient was kept under close observation for a while.

Numerous examinations of the gastric contents revealed conditions similar to those described. The paroxysmal attacks of pain became more frequent and intense. The pain was almost entirely in the epigastric region, which was now constantly tender to pressure. The stools were copious, of a mushy consistency, had a cadaverous odor, were extremely fatty and contained blood. Fat globules, fatty acid needles and fragments of striated muscle were abundant.

From a consideration of the nature of the stools, the paroxysmal pains in the epigastrium and the rapid emaciation, a diagnosis of chronic pancreatitis was made.

At operation on June 1, 1923 (performed by the late Dr. John W. Chambers), the liver was found normal; calculi were not detected either in the gallbladder or ducts. The stomach was fastened by adhesions to the under surface of the liver near the gallbladder; it did not contain masses. The pancreas was hard, firm and tense, giving a sensation as of scar tissue; at one point the pancreatic tissue was so hard that the presence of a calculus was suspected, which, however, was not found on closer investigation. The head of the pancreas was much enlarged. There was a definite chronic pancreatitis. Cholecystostomy was performed, and the patient made an uneventful recovery, gaining 42 pounds (19.1 Kg.) within a few months. When last seen (September, 1908), he was in good health.

CASE 3.—*Chronic pancreatitis with adhesions between the stomach and liver.*

Z. S., a man, aged 64, was admitted to the Church Home and Infirmary, on June 30, 1905, complaining of indigestion. The patient had suffered for the preceding year and a half with nausea, occasional vomiting, pressure and fulness following meals and pain in the epigastrium. The condition occurred irregularly, and was not dependent on the ingestion of food. Constipation was usually present and was often followed by attacks of diarrhea with copious stools. There was a great loss of weight and great weakness.

On physical examination, the patient appeared much emaciated; the heart and lungs were found to be normal. The abdomen was soft, enlargements or masses could not be detected. Analysis of the gastric contents after an Ewald test breakfast showed a total acidity of 45, free hydrochloric acid, 10. The urine was normal. The stools were large and soft; they contained much undigested fat and muscle fibers. The blood count showed: red blood cells,

5,096,000; leukocytes, 5,600; hemoglobin, 70 per cent; the differential count was normal.

From the age of the patient, his loss of flesh and the digestive disturbance, we concluded that we were probably dealing with carcinoma of the stomach, and an exploratory operation was determined on.

At operation adhesions were noticed between the stomach and liver, and the head of the pancreas was found hard and firm, presenting definite indications of a chronic pancreatitis. The adhesions were released; the gallbladder was drained, and the patient made a good recovery.

CASE 4.—*Chronic pancreatitis with gallstones and chronic appendicitis.*

S. C., a woman, aged 41, was admitted to the Church Home on April 22, 1908, with a history of having suffered during the preceding three years from acute attacks of abdominal pain, located under the right costal arch and radiating toward the right shoulder-blade. These occurred at irregular intervals, were frequently accompanied by chills and fever, and were occasionally followed by jaundice. During the last eight months, there had been much indigestion in the form of pressure and fulness following meals and not infrequently nausea and vomiting. The patient had lost 20 pounds (9 Kg.) in weight and complained greatly of weakness and of obstinate constipation.

On examination the heart and lungs were found normal. The abdomen was soft, the edge of the liver was palpable and tender to pressure.

Analysis of the gastric contents following an Ewald test breakfast revealed a total acidity of 22, free hydrochloric acid, 0. The urine was normal. The stools were large and bulky; they contained much undigested fat and muscle fibers. Examination of the blood did not present abnormalities.

The diagnosis of cholelithiasis with possible chronic pancreatitis was made, and an exploratory operation was advised. At operation the gallbladder was found enlarged and thickened. It contained from forty to fifty hard, dark, slightly faceted stones; these were removed, and the gallbladder was drained after removal of the appendix, which was considerably dilated and adherent throughout its length. The pancreas was much enlarged, firm and markedly indurated; it presented every evidence of being chronically inflamed.

CASE 5.—*Chronic pancreatitis in a woman with a duodenal ulcer firmly adherent to the head of the pancreas.*

A. B., a woman, aged 46, was admitted to the Church Home and Infirmary on May 22, 1913, with a history of indigestion extending over a period of at least six years. At first she had had much pain several hours after meals, which was usually relieved by the ingestion of food and by the use of alkalis. The appetite at times was good, but the patient was afraid to eat. A carefully regulated diet was then prescribed. The pain gradually disappeared, and distention began to manifest itself in the region of the stomach; during the past two years there had been nausea and vomiting. The latter was apparently of the retention type, and occurred at intervals of three or four days. During the past year, there had been obstinate constipation, alternating with diarrhea and the passage of copious stools.

When first seen, the patient appeared extremely weak and emaciated, and because of the distress due to the digestive disturbance she insisted on an operation.

Physical examination showed that the organs of the chest were normal. The abdomen was extremely relaxed. Tender areas or masses could not be made out,

but the stomach appeared prolapsed, and there were occasional evidences of peristaltic waves.

On exploration the stomach was found dilated and prolapsed, the lower border lying in the pelvis. The transverse colon was also greatly prolapsed. A definite duodenal ulcer with constriction was found in this region, and the duodenum was firmly adherent to the pancreas. The head of the pancreas was hard and firm, and there was every evidence that we were dealing with a chronic inflammatory process especially involving this portion of the organ.

A posterior gastro-enterostomy was performed, and then a Coffey operation in which the tissues between the stomach and transverse colon were brought together with ten black stitches, which were then fastened to the anterior abdominal wall. At the completion of the operation the stomach was in good position. The patient stood the procedure well, and made a satisfactory recovery.

CASE 6.—*Chronic pancreatitis with adhesions in the region of duodenum and gallbladder. Acute suppurative cholangitis and cholecystitis.*

F. J. S., a woman, aged 63, was admitted to the Church Home and Infirmary on April 15, 1914. Her general health had always been good, though she had had obstinate constipation for years. Her illness began in April, 1913, with diarrhea, which lasted for the entire summer, during which she lost 80 pounds (36.3 Kg.) in weight. In December, 1913, she had a sudden attack of acute pain in the upper right side of the abdomen, which radiated to the upper right side of the back and shoulder-blade. This was accompanied by nausea and vomiting and the pain was so intense as to require a hypodermic injection of morphine. The attack was followed by jaundice, and the patient was forced to remain in bed for three weeks. Following this the slightest indiscretion in diet induced similar attacks, so that recurrences occurred every two or three weks. On examination the patient presented evidence of great loss of weight; the thoracic organs were normal. The abdomen was flabby; the edge of the liver palpable and tender to pressure, and an indefinite mass was felt in the epigastrium.

An examination of the urine showed the presence of albumin, acetone, hyaline and granular casts. The examination of the blood showed: red blood cells, 4,100,000; white blood cells, 6,250; hemoglobin, 60 per cent; the differential count was normal.

From the history of marked loss of weight, the apparent attacks of cholelithiasis and the indefinite nodule in the epigastrium the probable diagnosis of carcinoma of the stomach and liver together with cholelithiasis was arrived at, and operation was advised.

On the following day a right rectus incision was made, and the stomach was found adherent over a mass just above the lesser curvature. There were recent adhesions in the region of the duodenum extending over the gallbladder. The gallbladder was thick and shrivelled. There was not any evidence of a mass in the stomach itself. The mass above the lesser curvature of the stomach was continuous with an enlarged and nodulated pancreas, and on further investigation appeared to form a part of it. The liver was much larger than normal, extending as far down as the umbilicus; it was free from any growth. It was evident that we were dealing with a chronic pancreatitis. The gallbladder was drained. It contained a small amount of pus, but did not contain bile or stones. One drain was passed down toward the lesser curvature of the stomach and two beneath the gallbladder. The patient seemed to do well for the first twenty-four hours, and then began to lose ground. She secreted only a small amount of urine; bronchopneumonia developed, and she died on April 17, 1914.

At autopsy the pancreas was found enlarged, measuring 13 cm. from head to tail. It was hard and firm; section showed that the lobulation was rather coarse, and there was an increased amount of gray translucent interlobular connective tissue. Areas of necrosis were not noted in the fat about the pancreas. The ducts were patent and contained much sero-sanguineous fluid. Additional evidences of an acute suppurative cholangitis and a subacute nephritis were present.

CASE 7.—*Marked case of chronic pancreatitis with enlargement of the liver in a patient affected with pulmonary tuberculosis.*

W. S., a woman, aged 59, consulted us on May 25, 1916, for indigestion which had been present for about ten or twelve years, but which had recently become greatly aggravated. She complained of a sense of fulness and distention after meals with occasional nausea. There had never been any violent attacks of pain in the abdomen, though there was almost constant discomfort. Diarrhea was of frequent occurrence, the stools often being copious and of an oily, greasy appearance. In addition, the patient had complained for a long time of cough and expectoration, and occasionally of fever, night sweats and extreme weakness.

On examination the lungs presented evidence of marked consolidation of both apexes; the heart was normal. The abdomen was distended; the edge of the liver was palpable and tender to pressure.

Analysis of the gastric contents following an Ewald test breakfast showed a total acidity of 23, free hydrochloric acid, 0. The stools were liquid, of a foul odor and contained large amounts of undigested fat and muscle fibers. The duodenal contents showed an absence of the trypsin ferment and a diminution in amount of the amylopsin and steapsin.

Roentgen-ray examination revealed a marked tuberculous consolidation of the apexes of both lungs. The gastro-intestinal series pointed to adhesions in the upper right quadrant.

The diagnosis of possible disease of the gallbladder with chronic pancreatitis was made, and an exploratory operation was advised.

At operation, the pancreas was found to be about three times its normal size and extremely hard. The edge of the liver near the gallbladder presented a puckered appearance as if from an old inflammation. The gallbladder was free from adhesions, but on account of the chronic inflammatory condition of the pancreas, it was drained. The tuberculous process did not appear in the abdomen. The patient stood the operation well and made a satisfactory recovery.

CASE 8.—*Chronic pancreatitis with a history of cholelithiasis followed by symptoms of indigestion, loss of weight and strength.*

B. W., aged 58, first consulted us on Sept. 5, 1916, for indigestion which had persisted for the preceding six years. He first had a sudden attack of acute abdominal pain located under the right costal arch and radiating toward the shoulder-blade on the same side. These attacks were accompanied by chilly sensations which were followed by fever. Several such attacks had occurred during the preceding few years. In addition to these attacks, there was more or less continuous abdominal distress, flatulence, pressure and fulness following meals, constipation alternating with diarrhea and great loss in weight, 35 pounds (15.9 Kg.), and strength.

On examination the patient was found to be poorly nourished and markedly emaciated. The mucous membranes were pale, the tongue was coated, the pulse weak and the blood pressure was, systolic, 110; diastolic, 55. The heart and lungs were normal. The abdomen was somewhat distended; the liver

slightly enlarged; masses were not noted on palpation and tenderness was not evident. Analysis of the gastric contents following an Ewald test breakfast showed achylia, total acidity, 25; free hydrochloric acid, 0. The urine was usually normal, but occasionally contained traces of sugar. The blood count showed: red blood corpuscles, 4,168,000; white blood corpuscles, 6,560; hemoglobin, 54 per cent; otherwise normal. Results of the Wassermann test were negative.

The stools were usually copious and frequent, from eight to ten a day; at times they were solid, but usually they were liquid, light and foul and contained much undigested fat and muscle fibers. Examination of the duodenal contents for ferments revealed that amylopsin was present, steapsin was absent, and that there was only a trace of trypsin. Results of a roentgen-ray examination were negative.

The diagnosis of chronic pancreatitis was based on a history of attacks caused by gallstones and indigestion, the nature of the stools, the occasional traces of sugar in the urine, the result of the analysis of the pancreatic secretion and the loss of weight and strength.

The patient lived for four years, during which there were periods of from one to two months of relief followed by serious recurrences of the symptoms noted above. Finally he succumbed following an exhausting diarrhea.

CASE 9.—*Chronic pancreatitis in a patient with cholelithiasis. Pancreas nodular and twice its normal size.*

H. L., a woman, aged 48, was admitted to the Church Home and Infirmary on May 17, 1919. For the preceding five or six years, she had had indigestion in the form of pressure and fulness after meals and marked distention; occasional nausea and vomiting occurred. During the year before, there had been a number of acute attacks of abdominal pain, beginning beneath the right costal arch and radiating toward the right side of the back and shoulder-blade. The pain was so intense as to require hypodermic injections of morphine for relief. These attacks were accompanied by chills and fever, as well as nausea and vomiting, and were followed by jaundice. In the three months before she came to the hospital the condition had materially changed. During this period epigastric pain had been almost constant, though severe at times and slight at others; it had radiated to the left side and was associated with frequent nausea, vomiting and extreme weakness. The patient had lost 30 pounds (13.6 Kg.) and was slightly jaundiced. On examination, the organs of the chest were found normal. The abdomen was soft, and there was a marked tender area in the midepigastrium extending toward the left side. A definitely tender area was also noted in the right lower quadrant with muscle spasm in this region.

The urine was normal except for a trace of bile. The diagnosis of cholelithiasis with chronic appendicitis was made, and operation was advised. On May 19, 1919, a McBurney incision was first made, and the appendix was removed. It was found thickened near its tip, and the cecum was bound down by old adhesions.

A right rectus incision was then made, and a marked thickening and enlargement of the pancreas was noted; it was nearly twice its natural size and extremely nodular. In the gallbladder there was a composite stone consisting of a number of small ones that had been fused. It reminded one of a piece of broken concrete. Further stones were not observed, and there was no thickening of the walls of the gallbladder. The gallbladder was drained. The patient

made an uneventful recovery, and was discharged on June 13, 1919, in good condition.

CASE 10.—*Chronic pancreatitis with gallbladder adhesions and enlarged lymph glands along the common duct.*

G. M. H., a woman, aged 18, admitted to the Church Home and Infirmary, on May 16, 1922, had formerly been in excellent health with a good appetite and without indigestion; constipation had, however, been present since childhood. Her illness began during the later part of January, 1922, with nausea and gradually increasing jaundice. The stools were copious, extremely constipated and of an ashy gray. She did not have any pain. Following this attack, the duration of which was about two weeks, the jaundice cleared up, and the patient was apparently in good health until March 15, 1922, when she had the "grip," which lasted over a period of two weeks. Following this she again became jaundiced, and remained so.

On physical examination, the heart and lungs were found normal. The abdomen was symmetrical, the liver was palpable just beneath the costal arch and was firm and tender. Other tender areas were not noted.

The urine was normal, except that it contained much bile. The stools were large, slate-colored, and contained much undigested fat and muscle fibers.

From the long-continued and painless jaundice, together with the bulky stools containing undigested fat and muscle fibers, the diagnosis of chronic pancreatitis was considered.

The patient was given several preliminary intravenous injections of calcium chloride and was operated on, May 27, 1922.

A right rectus incision was made, the gallbladder exposed and found to be small. Numerous adhesions were noted between the gallbladder and duodenum and omentum. These were liberated. A chain of enlarged lymph glands was observed along the common duct, some of them 1 cm. in length and 1 cm. in breadth, and the pancreas was found much enlarged as well as hard and nodular. The gallbladder was incised and drained with a small rubber tube and two cigaret drains placed beneath the gallbladder. Evidence of gallstones was not present. The patient made an uneventful recovery and was discharged from the hospital in good condition on June 21, 1922. She was still well on Nov. 16, 1926.

CASE 11.—*Chronic pancreatitis simulating carcinoma of the head of the pancreas. Relief under medical treatment.*

S. S., a man, aged 76, consulted us on Sept. 10, 1923, for a digestive disturbance from which he had suffered for more than three months and prior to which he had always enjoyed good health. He complained of diarrhea, discomfort in the epigastrium, occasional nausea, extreme weakness and a loss of 22 pounds (10 Kg.) in weight. The stools numbered about five a day and occurred mainly in the morning. They were extremely bulky, oily, soft and fetid.

On physical examination the patient presented the appearance of having lost considerable flesh; he was somewhat anemic, and the conjunctivae showed a slight icteric tint. His thoracic organs were normal; his blood pressure was systolic, 155; diastolic, 80.

The abdomen was soft; the liver was slightly enlarged, and its surface was smooth; the spleen was not palpable. Tender areas or masses were not noted.

A gastro-intestinal roentgen-ray study did not reveal any defects in the stomach or duodenum. The duodenum, however, was pulled over and held

firmly under the region of the liver by adhesions. Other abnormalities were not found.

The examination of the urine revealed a trace of bile, and sugar intermittently, but it was otherwise normal. The stools were soft and bulky, and characteristically showed much undigested fat and muscle fibers. The blood count was as follows: red blood cells, 4,100,000; white blood cells, 5,160; hemoglobin, 62 per cent; differential count, normal. The Wassermann reaction was negative.

A chemical test of the blood gave negative results with the exception of the blood sugar, which on several occasions reached 0.13 per cent in the fasting state, while at other times it was normal.

It was impossible at first to determine whether we were dealing with a chronic pancreatitis or cancer of the head of the pancreas.

However, under a carefully regulated diet and rest, the stools became less frequent, and the patient gradually regained 15 pounds (6.8 Kg.) in weight. He still at times had recurrences of diarrhea with the characteristic stools and glycosuria, which extended over a period of five or six day to a week, but which were always relieved by care in diet and rest. After more than three years since this patient manifested his first symptoms, he was in good condition. This must definitely exclude the presence of carcinoma.

CASE 12.—*Chronic pancreatitis with a history of indigestion and acute abdominal pain followed by jaundice, apparently from the gallbladder. Diarrhea; absence of pancreatic ferments. Improvement.*

A. R., a man, aged 69, was admitted to the hospital on Jan. 28, 1926, complaining of indigestion. During the previous few months he had had attacks of indigestion characterized by acute pain in the upper part of the abdomen, radiating toward the right shoulder-blade and followed by jaundice. The attacks would appear at irregular intervals, were sufficiently severe to require hypodermic injections of morphine and were frequently accompanied by chills and fever. Recently there had been diarrhea with six or eight liquid stools a day. The patient had lost much strength and flesh.

On examination the skin and sclerae were found to be extremely jaundiced. The thoracic organs were normal. The abdomen was markedly distended and the liver enlarged. Tenderness was not felt. The urine was examined frequently and revealed the presence of sugar at intervals. Examination of the blood gave the following results: red cells, 4,200,000; white cells, 9,150; hemoglobin, 84 per cent; differential count, normal; Wassermann test, normal; blood chemistry, normal. The roentgen-ray examination revealed adhesions in the upper right quadrant. The gastric analysis showed a total acidity of 20 and an absence of free hydrochloric acid, after an Ewald test breakfast. The stools were large, soft or liquid, and contained much undigested fat as well as many fibers. An examination of the duodenal contents showed a total absence of the steapsin and trypsin ferments; amylopsin was present in normal amounts.

The patient was placed in bed and given a liquid and soft diet. Treatment consisted of daily nonsurgical biliary drainages according to the Lyon method. The pain gradually subsided; the jaundice disapppeared; there was a gain in weight, and his general condition became much improved. After ten months, however, he continued at times to pass bulky, oily stools.

In chronic pancreatitis there is an increased production and thickening of the interstitial tissue of the pancreas with destruction of the glandular

substance. Ordinarily, the increase in connective tissue is primary and may be diffuse, involving the entire gland, or may be limited to certain areas. There are two well recognized types of this condition—the interlobular and the interacinar forms. In the first variety the interlobular connective tissue is greatly increased and thickened, and the glandular structures are compressed. In the second, diffuse areas or bands of connective tissue are formed which penetrate within the glandular acini and separate them, while the interlobular tissue is only slightly invaded.

According to Opie,[24] of thirty cases of chronic pancreatitis occurring at the Johns Hopkins Hospital, twenty-one represented the interlobular and nine the interacinar type.

The interlobular form occurs as a result of occlusion of the pancreatic duct or as a result of infection caused by calculi situated in the biliary or pancreatic passages, and is caused by such organisms as the colon bacillus, streptococci or occasionally the typhoid bacillus. As the disease progresses, fibrous tissue in large amount may be produced, the entire gland being converted into a narrow band of connective tissue surrounding a duct containing calculi. At this stage many lobules are destroyed, and the acini within become atrophied. The islands of Langerhans are less affected at this stage, but as the disease progresses, they are finally damaged by the pressure, and disturbances of the blood supply, and atrophy takes place.

In the acinar variety of chronic pancreatitis, the gland is less hard and nodular than in the interlobular form. There is a diffuse fibrosis between the acini, the interlobular tissue being but slightly involved. Even in its early stages, there is involvement of the islands of Langerhans. These are surrounded by connective tissue which separates them from surrounding structures, and within the islands bands of connective tissue and the increased fibrous proliferation bring about an atrophy of the cells of the island which finally leads to their destruction and replacement by connective tissue. In a considerable number of instances, there is a definite sclerosis of the arteries.

Chronic interacinar pancreatitis is usually a result of infection, and is produced by such conditions as cirrhosis of the liver, alcoholism and arteriosclerosis. Its etiology in some instances, according to Opie, is obscure. In chronic interlobular pancreatitis the infection is usually introduced through the duct of the gland, while in the interacinar form the infection is probably introduced through the blood supply.

In hemochromatosis, which is associated with chronic pancreatitis, the most prominent lesion is in the interacinar tissue and islands of Langerhans; in addition, there is an increase in the interlobular connective tissue.

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24. Opie, in Osler: Modern Medicine, ed. 3, Philadelphia, Lea & Febiger, 1926, vol. 3, p. 686.

According to Opie,[24] of thirty cases of chronic pancreatitis observed at the Johns Hopkins Hospital, seventeen were noted in men and thirteen in women. The disease occurs largely between the ages of 40 and 60. In our series of fifteen cases there were eight men and seven women, the ages ranging between 18 and 76, the greatest number (twelve) occurring between 40 and 70.

The relation of cholelithiasis to chronic pancreatitis has been a matter of considerable interest; for chronic pancreatitis has not uncommonly been noted at operation for gallstones. Opie [24] considers that this relationship can exist, even though the pancreatic duct is not occluded with calculi. It is probable that in these cases the infection spreads from the biliary passages to the pancreatic duct or from the duodenum. Though infection through the lymphatics has been noted by Deaver and Sweet,[25] Opie claims that definite proof of its occurrence has not yet been established.

It is interesting in this connection to note that Deaver and Pfeiffer [26] have demonstrated disease in the pancreas in 33 per cent of all cases of cholecystitis, and that chronic pancreatitis has frequently been observed as a secondary development following a cholecystectomy.

Symptoms.—Until a comparatively few years ago, this condition was considered rare, as many cases escaped recognition; but with the greater precision in diagnosis, together with the aid afforded by newer laboratory procedures, many more cases should now be recognized. The diagnosis of chronic pancreatitis is frequently based on the firmness and hardness of the head of the pancreas noted on palpation at operation. In some instances, however, as has been pointed out by Pratt and verified by Deaver, this condition may be merely a temporary swelling due to congestion.

Although the symptoms are rarely definite, chronic pancreatitis should be suspected in a patient presenting a chronic dyspepsia, with or without a history of biliary colic, if he complains, in addition, of a severe or slight epigastric pain situated often to the left of the midline and also referred to the left shoulder-blade, associated with nausea, vomiting, emaciation, extreme weakness, slight jaundice and occasionally with ptyalism and stomatitis. Occasionally, the pancreas may be palpated, and may be tender to pressure.

In certain instances intermittent glycosuria, hyperglycemia, bulky, soft and fetid stools aid in arriving at the diagnosis. The stools in these cases number from four to eight daily, usually occur in the morning and

25. Deaver and Sweet: Prepancreatic and Peripancreatic Disease, with a Consideration of Anatomic Basis of Infection from Gallbladder to Pancreas, J. A. M. A. **77**:194 (Jan. 19) 1921.

26. Deaver and Pfeiffer: Tr. Am. Surg. A. **39**:121, 1921.

contain undigested fat and undigested protein in the form of striated muscle fibers.

It is interesting to note that in our series of fifteen cases of chronic pancreatitis, there was a history of chronic dyspepsia in eleven; biliary colic in five; epigastric pain in five; extreme loss of weight in nine; marked weakness in seven; jaundice in seven; ptylaism in two; intermittent glycosuria in three, and diarrhea with fatty stools in twelve.

Many of the symptoms are often lacking, and consequently the diagnosis becomes extremely difficult, as the condition does not have any characteristic pathognomonic symptom. In drawing conclusions, therefore, great stress must be placed on the history of gastro-intestinal disturbances occurring with slight jaundice, progressive loss of weight and strength and the appearance and nature of the stools.

Great assistance in diagnosis may sometimes be derived from the examination of the duodenal contents for pancreatic ferments, for in chronic pancreatitis their activity is markedly diminished. By means of the method devised by McClure, Wetmore and Reynolds,[27] accurate studies of this secretion have been made in normal persons and in some affected with chronic pancreatitis. According to Silberman and Denis,[28] who used the same method, normal persons present an enzyme activity of lipase of from 0.8 to 2 mg.; amylase, from 1.3 to 2.6 mg.; protease, from 1.3 to 2.9 mg. In patients with chronic pancreatitis the following figures were noted: lipase, from 0.1 to 0.8 mg.; amylase, from 0 to 0.8 mg.; protease, from 0.2 to 1.6 mg.

Bassler [29] has worked out a quantitative test for pancreatic activity which is easily applied clinically. After much experimentation, he has concluded that the amylase is the most satisfactory ferment in testing for pancreatic activity. His method may be utilized with advantage for the detection of changes in the pancreatic secretion in cases of chronic pancreatitis. But although these methods of laboratory investigation may be extremely helpful in the diagnosis of chronic pancreatitis, the evidence afforded by the study of the duodenal contents must always be interpreted with caution.

Diagnosis.—In the differential diagnosis, the following conditions must be considered: cancer of the head of the pancreas, cancer of the common bile duct, cancer of the liver and stones in the common duct.

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27. McClure, Wetmore and Reynolds: New Methods for Estimating Enzymatic Activities of Duodenal Contents of Normal Man, Arch. Int. Med. **27**:706 (June) 1921, and Am. J. M. Sc. **167**:649, 1924.

28. Silberman and Denis: South. M. J. **17**:549, 1924.

29. Bassler: Quantitative Test of Digesting Pancreatic Activity, Easily Applied Clinically; Tests for Volume of Pancreatic Juice and Bile Secretions, Arch Int. Med. **35**:162, 1925.

In cancer of the head of the pancreas, the onset is gradual without pain, and when jaundice manifests itself, it remains constant and deepens. The feces are bulky, however, and contain large amounts of undigested fats. There is extreme and progressive loss of weight with anemia and finally edema of the extremities and ascites. The differential diagnosis is, however, extremely difficult in many instances, and even at operation, it is not unusual to arrive at the erroneous conclusion of cancer of the head of the pancreas when the condition is actually a chronic pancreatitis. At times when operating for gallstones, the surgeon discovers a large, hard and often nodular mass in the region of the head of the pancreas, which will lead to the diagnosis of cancer. A similar conclusion may be reached in certain instances in which there has been marked loss of flesh, jaundice without pain and with fatty stools. His diagnosis is frequently incorrect, though his treatment may be correct; the hard nodular mass may be due to a chronic pancreatitis, in which case drainage of the gallbladder will bring about recovery, or at least improvement.

The three following cases with similar histories illustrate this condition:

CASE 13.—*Chronic pancreatitis with attacks of cholelithiasis.*

L. M., a man, aged 52, gave a history of attacks of cholelithiasis extending over a period of three years. These attacks appeared irregularly, and were violent at times, although the patient enjoyed good health in the intervals. The last attack, which had occurred four weeks previously, was somewhat unlike the others. The pain was less violent, and was located in the epigastrium. Chills and fever were present, and jaundice followed within a few days. The fever, however, gradually subsided, but the jaundice continued. Constipation, which was present at first, gradually disappeared and was followed by diarrhea. The patient had lost about 20 pounds (9 Kg.) in weight. Physical examination at this time revealed a tenderness under the right costal arch, but a mass could not be detected. A diagnosis of cholelithiasis with involvement of the common duct was made. At operation stones were found in the gallbladder and in the common duct. The head of the pancreas was much enlarged, firm and hard. The conclusion was reached that we were dealing with a cancer of the head of the pancreas with cholelithiasis. The stones were removed, and the gallbladder was drained. The patient had a stormy convalescence from the operation, and continued to lose weight. During the following weeks attacks of diarrhea occurred with profuse, greasy stools in which much undigested fat was noted. After four weeks, however, these conditions subsided, and there was gain in weight; the jaundice entirely disappeared, and the patient has continued in good health.

CASE 14.—*History of indigestion, jaundice, extreme constipation, much loss of weight, diminution of pancreatic ferments. Diagnosis of cancer of head of pancreas.*

T. S., a man, aged 61, had always been in good health until the onset of this illness. About three months before he came to the hospital he began to complain of indigestion, nausea, occasional vomiting and discomfort following meals. About four weeks before he was admitted to the hospital he first noted

the onset of jaundice, which gradually became marked. Constipation had been obstinate, and he had lost 15 pounds (7 Kg.) in weight.

Examination of the abdomen did not reveal tenderness, enlargement or masses. The gastric secretion at this period showed an absence of free hydrochloric acid, and the duodenal contents a diminution of its ferments (trypsin and amylopsin). An attempt to obtain bile by means of nonsurgical biliary drainage was unsuccessful. The diagnosis of carcinoma of the head of the pancreas was made. At exploratory operation the gallbladder was found apparently normal, and did not contain stones. There was a single stone in the common duct. The head of the pancreas was hard and nodular, and on palpation gave a distinct impression of carcinoma. The common duct stone was removed, and the duct and gallbladder were drained. The jaundice disappeared within a few weeks, and the patient made an uneventful recovery and has since been well.

CASE 15.—*Chronic pancreatitis with indigestion followed by jaundice and diarrhea with large, fetid, fatty stools; loss of weight. Diagnosis: Cancer of the head of the pancreas.*

F. L., a man, aged 56, had enjoyed good health until five months previously. He then began to complain of indigestion in the form of pressure and fulness after meals, nausea and occasional vomiting. The indigestion had gradually increased, and within the last month the patient had been jaundiced. Since then there had been diarrhea with the passage of five or six large, fetid, fatty stools occurring mainly in the morning. He had lost 30 pounds (13.6 Kg.) in weight.

On physical examination nothing abnormal could be detected in the abdomen. The diagnosis of probable carcinoma of the head of the pancreas was made. At exploratory operation evidence of stones in the gallbladder or duct could not be detected. The head of the pancreas was hard and firm. The gallbladder was drained, and the diagnosis of carcinoma of the head of the pancreas supposedly was confirmed. The patient, however, made an uninterrupted recovery. The jaundice disappeared, and he has since gained 45 pounds (20.4 Kg.) in weight, and is in splendid health.

Cancer of the common duct is frequently accompanied by gallstones, and if the disease extends to the papilla, the symptoms may be much like those observed in chronic pancreatitis.

In cancer of the liver, the nodulated areas on the surface of this organ and its rapid enlargement aid in differentiating it from chronic pancreatitis.

The differential diagnosis from cholelithiasis is at times difficult, especially in instances of chronic pancreatitis that are associated with paroxysmal pain. While these attacks are similar to those noted in cholelithiasis, the pain is usually less intense. The tenderness is more likely to be situated in the epigastrium, and the pain radiates toward the left shoulder-blade. The stools do not present the great excess of fat in cholelithiasis usually noted in chronic pancreatitis. As chronic pancreatitis is so frequently associated with gallstone disease, the presence of typical symptoms of cholelithiasis may be of value as pointing to the necessity of early operation, at which both conditions may be corrected.

Prognosis.—The prognosis of chronic pancreatitis is ordinarily not unfavorable if the disease is recognized sufficiently early to forestall serious injury to the pancreas. The greater the destruction of the gland, the more unfavorable is the prognosis. In many instances the morbid progress of the disease is slow, and many months or years may elapse before definite signs of it are manifested. The causes of death from this condition are usually progressive loss of flesh and exhaustion, hemorrhage or diabetes.

Treatment.—Robson and Cammidge [28] correctly point to the prophylactic treatment of this disease, especially by the early removal of gallstones before complications have been produced. Such conditions as duodenal catarrh and inflammation of the biliary passages should also be overcome by means of appropriate treatment. As preventive measures for these conditions, as well as for the treatment of the milder forms of chronic pancreatitis, the following procedure should be prescribed. The patient should be placed on a carefully regulated diet, with small meals at regular intervals not too far apart. Prolonged fasting should be avoided, for the process of eating increases the flow of bile and of pancreatic juice, and on this account it is well for the patient to take an additional light meal at night. Fats should be reduced to a minimum, while, on the other hand, carbohydrates should be consumed in increased amounts. Too much meat should not be eaten, and only the lean part should be used. Milk is permissible, and green vegetables and fresh fruits may be partaken of freely. Cereals and stale bread are also useful foods in this condition. Alcoholic stimulants must be forbidden, while coffee and tea may be taken moderately, and tobacco should be avoided or the amount used greatly reduced. The drinking of large amounts of water, and the free use of alkaline mineral waters are indicated.

Since Rothchild and Rosenthal have shown that hypercholesterinemia exists in cases of cholelithiasis, it is well, in the management of cases of pancreatitis dependent on gallstone disease, to lessen the cholesterin content of the food as far as possible, both before and after operation. This can be accomplished by placing the patient on a fat-free diet; all foods rich in fats should be excluded, as butter, olive oil, cream and eggs.

In addition to keeping to his diet, the patient should avoid overexercise, and should be given occasional purges of calomel or frequent alkaline salines.

Nonsurgical biliary drainage according to the Lyon method will do much, by avoiding or overcoming infection in the biliary tract, duodenum and pancreatic duct, to prevent the onset of this serious disease. This method of treatment is especially applicable when there is infection in these passages without the presence of stones. The impaired pancreatic function may be aided at times by the administration of pancreatic preparations. If, after a thorough trial of the treatment outlined, the symp-

toms persist, surgical intervention must be considered, especially if gallstones are present, and there is persistent jaundice.

In the surgical treatment of this disease, the cause should be eradicated as far as possible. If gallstones or pancreatic stones are present, they should be removed, if possible, and infection should be overcome. It is always important to secure adequate and effective drainage of the biliary and pancreatic passages by means of cholecystostomy, cholecystenterostomy or gastrocholecystostomy.

If the cause can be completely removed at an early stage, at least a clinical cure may be expected. Even in advanced cases, an arrest of the pathologic process may be hoped for, and the nonaffected portion of the pancreas may carry on the function of the gland, though perhaps to a lesser degree.

Inasmuch as it is difficult to overcome the infection entirely in all instances, even by surgical measures, occasional nonsurgical biliary drainages may be continued with advantage after operation in order to avoid recurrences.

SUMMARY

The incidence of both acute and chronic pancreatitis is far greater than has generally been recognized, and as the symptomatology of these conditions is usually indefinite, the correct diagnosis is too rarely made. In acute hemorrhagic pancreatitis the onset is ushered in by a sudden violent pain in the epigastrium, with signs of shock, which may suggest rupture of a peptic ulcer, gallbladder or even of the appendix. It may be followed by death within a few hours or days. The acute gangrenous form follows the hemorrhagic type, in which the symptoms manifested have been of a milder or subacute form. This condition manifests itself by the appearance of chills, fever and the formation of a mass in the epigastrium within a week or two after the onset of the hemorrhagic stage. The acute suppurative type, in which abscesses are formed, frequently ensues as a subsequent stage after either of the two types first named. It is associated with chills, fever and frequently with jaundice, nausea, vomiting and severe epigastric pain. Attention must be directed particularly to the significance of fat necrosis as an important accompaniment, especially of hemorrhagic and gangrenous pancreatitis, and its value as a diagnostic sign at operation. Owing to the great operative risk, the question as to whether immediate surgical intervention should be undertaken has not as yet been definitely established in cases of acute hemorrhagic pancreatitis. Many surgeons consider that it is best to delay until shock has somewhat subsided. Each case must be considered separately; a routine rule cannot be laid down. When the disease has progressed to the gangrenous and suppurative stages, speedy operation is indicated.

In the study of chronic pancreatitis, the relation of this condition to cholecystitis and cholelithiasis is a matter of considerable interest. Although the symptoms of chronic pancreatitis are rarely definite, its presence should be suspected if, in a patient who has suffered from a chronic dyspepsia with or without a history of biliary colic, there is present a severe or slight epigastric pain associated with nausea, vomiting, emaciation, extreme weakness, slight jaundice and, occasionally, with ptyalism and intermittent glycosuria. In many instances the bulky, soft, fetid and oily stools containing undigested fat and protein aid in arriving at the diagnosis. Great assistance may be rendered in diagnosis by an examination of the duodenal contents for pancreatic ferments, which may be markedly diminished in their activity in this condition.

In the diagnosis, difficulty may be experienced in differentiating between cancer of the pancreas and chronic pancreatitis. Even at operation, cancer of the pancreas is sometimes diagnosed when the condition is actually a chronic pancreatitis.

In the prophylactic treatment of this condition, attention must be especially directed to the early removal of gallstones before complications have occurred and, as preventive measures, a carefully regulated diet should be followed, together with nonsurgical biliary drainages to avoid or to overcome infection in the biliary tract and prevent the onset or progress of this serious disorder. When the disease is definitely established, immediate operation is advised. If gallstones or pancreatic stones are present, they should be removed and infection overcome. It is important to secure effective drainage of the biliary passages by means of cholecystostomy, cholecystenterostomy or gastrocholecystostomy.

OSSIFYING FIBROMAS OF THE JAW

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The region of the jaw may be the site, not only of those peculiar tumors which are associated with the formation of the teeth, but also of most of the tumors which occur in other parts of the body. Of the latter group, the fibroma is probably the most frequent. In rare instances it has been observed to be associated with ossification and has been termed an osteofibroma. As a review of the literature has revealed only fourteen of these cases, it may be of value to point out some of the characteristics in connection with three cases which have come under my observation.

REPORT OF CASES

CASE 1.—M. D., an Italian girl, aged 12, entered the Children's Memorial Hospital on April 2, 1925, complaining of a lump on the right side of her jaw. The swelling had first been noticed about a year before and had grown steadily. It had never caused any pain or discomfort. Her family and past history was negative.

Physical Examination.—She was a well built, healthy looking girl. On the outer side of her right jaw was a hemispherical mass about 1 inch (2.5 cm.) in diameter. The mass was hard and firmly fixed to the ramus of the jaw near the angle. The surface of the mass was smooth and not tender to palpation. Blood examination showed 10,000 white blood cells. The Wassermann reaction was negative. Her pulse rate and temperature were normal. A series of roentgenograms of the jaw showed an area of increase bone penetration, circular in outline, in the anterior third of the right side of the jaw. This area was suggestive of a bone cyst.

Operation and Course.—On April 3, 1925, under ether anesthesia an incision was made over the tumor from the inside of the mouth, in the mucous membrane at the base of the lip. The mucous membrane was stripped back, exposing the bony tumor. A chisel applied to this bone revealed a soft mass of tumor tissue lying in a bed of the jaw bone and covered by a thin layer of bone. A capsule was not seen, but the tumor was easily removed, leaving a clean base. The tumor tissue was cream colored, homogeneous and hyaline in appearance, and friable. It was not vascular, but looked much like a sarcoma. The bed of the tumor, however, looked so smooth, and the removal of the tumor, although not encapsulated, appeared to be so clean cut that further excision did not seem to be warranted. The bed of the tumor was cauterized with phenol and packed with iodoform gauze.

The wound healed, and the child was discharged from the hospital clinic three weeks after operation. Eleven months after operation she was again examined, and evidences of recurrence could not be seen on physical examination or in roentgenograms.

Pathologic Examination by Dr. W. Hibbs.—Paraffin sections of the tumor tissue were stained with hematoxylin and eosin. All of the sections were essentially similar. About nine-tenths of the entire tissue consisted of densely ramifying, well-stained strands of adult connective tissue fibers. These

strands generally were from 5 to 12 fibers thick, and their course ran in many directions. Blood vessels were scarce, and those present had clumps of small round cells adjacent to them.

At the distal portions of all sections, the entangling fibrous tissue strands intimately surrounded islands of new bone formation of various shapes. The shape of these varied from round clumps of from 3 to 5 cells, to irregular trabeculae of bone from 2 to 3 cells thick, and from 15 to 20 cells long. Red blood cells infiltrated the tissue only in clumps adjacent to the islands of new bone formation. A capsule was not present (figs. 1 and 2).

CASE 2.—W. N., a white man, aged 66, entered the Presbyterian Hospital on Sept. 6, 1922. He said that forty-seven years previous to examination he had

Fig. 1 (case 1).—Osteofibroma of the lower jaw; low power magnification.

had a swelling of the lower right cheek that discharged pus for a long time. It had finally healed, and had not caused further trouble. Twelve years before, the patient had noticed a nodule growing on the upper jaw just inside the line of the teeth. The nodule was painless, but grew rapidly. The mass was removed by a surgical operation, and the patient did not have any trouble until about seven months before he was admitted to the hospital, when he noticed that his "jaw was swelling up." Since then, the swelling had increased steadily but without pain. His general health had been good, and he had not lost weight.

Physical Examination.—The patient was a well nourished man with a swelling in the right jaw, but apparently was not acutely ill. In the upper part of the right jaw there was a hard, immovable mass in the region of the molar teeth. The surface of this mass was somewhat ulcerated, but it was not tender to palpation. The right upper molar teeth were absent, and the remaining

teeth were in bad condition. Palpable glands were present in the left anterior triangle, and one could be felt on the right anterior triangle of the neck. There was a marked inguinal adenopathy on both sides. His temperature and pulse rate were normal. Results of the examinations of the urine and of the blood, including the Wassermann test, were negative.

Roentgenographic Examination.—Evidences of the formation of new bone were present in the region of the right maxillary antrum, irregular in density and outline, forming a new growth that extended upward, involving the antrum, and downward into the mouth through the upper jaw. The growth extended almost to the floor of the orbit.

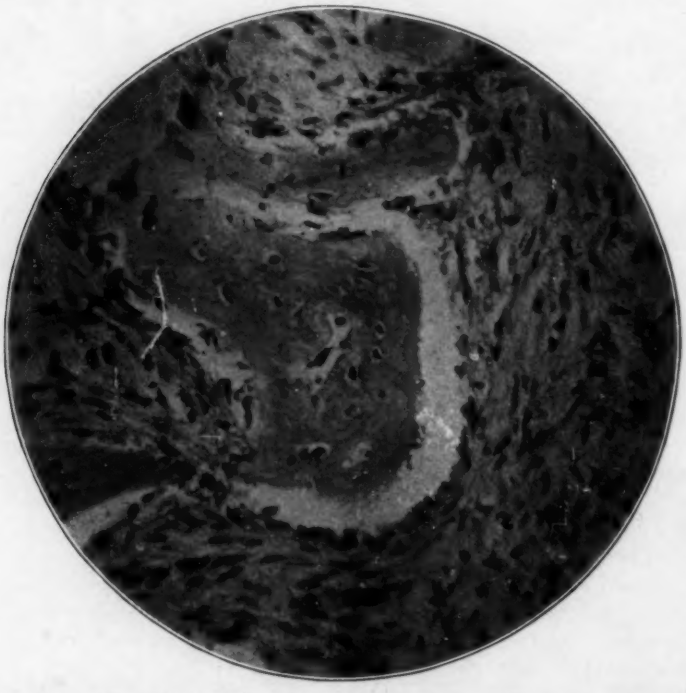

Fig. 2 (case 1).—Osteofibroma of the lower jaw; high power magnification.

Operation and Course.—On Sept. 9, 1922, this patient was operated on by Dr. A. D. Bevan. Under ether anesthesia, the right external carotid artery was ligated above the site of the superior thyroid through a small incision in the side of the neck. The tumor was exposed by an incision, extending from the middle of the upper lip to the nasal septum, then laterally around the wing of the nose and upward along the side of the nose to a point about 2 cm. from the lower edge of the orbit. From that point the incision extended outward, parallel to the orbital edge, to the external angle of the eye. The flap of soft parts marked out by the incision was dissected from the bone and reflected laterally. The maxillary bone, with the tumor mass, was separated from its attachments, and was removed, with the exception of the portion which formed the floor of the orbit. The space left by the removal of the tumor was packed with iodoform gauze, and the flap of soft parts was sutured back into place.

The wound healed, and two weeks after operation the patient was discharged from the hospital. The cavity into the mouth was clean and granulating. The patient had a complete postoperative paralysis of all the branches of the right facial nerve below the level of the orbit.

Pathologic Report (Dr. H. Oberhelman).—Microscopic examination showed that in one section of this tumor there was a network of delicate collagenic fibers of varying density. In places they assumed a whorllike arrangement. In this network there were elongated and many spindle-shaped, deeply staining nuclei, which were densest where the collagenic fibers were most compact. In places two, three or even four of the elongated nuclei were grouped, simulating in part, giant cells. There were also round cells, in places aggregated, elsewhere more diffuse. The entire section was relatively avascular, the lymphatic channels being more numerous than the blood vessels.

In another section there were skin and subcutaneous tissue along one side. The latter was dense, although in places it contained many fat spaces. The dense tissue was continuous with periosteum, and this in turn gradually shaded into bone made up of trabeculae. These anastomosed variously and enclosed for the most part fat spaces, but many contained concentric layers of spindleshaped cells and collagenic fibers, gradually shading into bone.

In another portion there was a collection of polymorphonuclear leukocytes, round cells and plasma cells in a background of many fibroblasts which diminished peripherally and gradually merged into bone. In this place and somewhat eccentrically placed, there was the root of a tooth surrounded by a dense connective tissue capsule.

Case 3.—T. S., an Italian laborer, aged 62, entered the Presbyterian Hospital on Jan. 2, 1917. He complained of a swelling in the upper jaw, with inability to close the mouth tightly. The first symptom of this trouble was a severe pain in the pharynx, associated with swelling in the neck. This attack occurred eighteen years previous to his coming to the hospital and lasted for four days. It was not severe enough to confine him to bed or to require drugs for relief. One year later he had an attack of rheumatism in the right arm and leg which lasted for thirteen months. A year after he recovered from this illness, he noticed a small, red, painless, soft swelling about the size and shape of a lima bean behind the upper incisor tooth. This swelling had increased to the size of a pigeon's egg within four years, and he had had the mass removed at the County Hospital. Just previous to this operation all his teeth had been extracted. Four years before he came to the Presbyterian Hospital he had had a severe, uniform, red swelling on the right side of his face, which had disappeared under hot applications after ten days. For the past two years, he had been unable to bring his jaws together tightly, and had had a slight pain in the left upper bicuspid region, radiating over the entire left cheek. He had had a growth in the cheek for twelve years, similar in type to the previous one which was removed. The growth was not painful unless it was traumatized.

His general health had always been good except as noted above. During the past twelve years he had gained 10 pounds (4.5 Kg.). He smoked a wooden pipe with strong tobacco and drank three or four glasses of wine daily. His history, otherwise, was negative.

Physical Examination.—The patient was a well developed white man without abnormalities except in the region of the upper jaw. A mass, which measured 5 cm. across, extended from the midline of the upper jaw laterally to the left. The surface of this mass was hard, smooth, and slightly tender to pal-

pation, without any evidences of fluctuation. The mucosa over the entire mass was red, rough and irregular. The mass appeared to have a definite border, and could be readily outlined.

Operation and Course.—On Jan. 4, 1917, under ether anesthesia, an incision was made in the mucuous membrane over the tumor mass, and most of the tumor was enucleated along the line of cleavage with a periosteotome. The remainder of the mass was curetted out, and an iodoform gauze pack was inserted.

The cavity healed rapidly under gauze packings, and the patient was discharged from the hospital on Jan. 12, 1917, with a small discharging sinus. The wound healed completely in a short time, and has not recurred up to date.

Pathologic Report (Dr. H. Oberhelman).—Microscopic examination of a typical section of the tumor of the superior maxilla showed many elongated pale-staining nuclei, others spindle-shaped and still others round. All were widely scattered in a moderately loose, network-like arrangement of collagenic fibers. In some places, these fibers were compact, and were arranged in wavy bundles, between which there was considerable extravasated blood in some areas. Along one side of the section, there were irregular islands of trabeculated bone. These islands lay in, and were closely associated with, the loosely arranged collagenic fibers, but in a few places tonguelike projections of these bony trabeculae were continuous with the more compact wavy bundles of connective tissue, gradually shading into the loosely arranged collagenic fibers. Bone marrow was absent from the spaces formed by the bony trabeculae, the spaces being occupied by the collagenic fibers. The tissue was relatively avascular. Some of the prominent blood vessels lay in the center of the loose tissue in the enclosed trabecular spaces.

In two or three places there were dense collections of small, deeply-staining nuclei, well demarcated from the surrounding tissue. These were not unlike giant cells. They also resembled small obliterated blood vessels. In one place these nuclei formed a column resembling a longitudinal section through such a blood vessel.

ABSTRACTS OF CASES FROM THE LITERATURE

CASES 4, 5, 6 AND 7 (Hildebrand, quoted by Hippel[1]).—"In rare cases fibroma formation is combined with the osteoma. Then between the bony trabeculae are found strands of spindle cell fibrous tissue, and the impression is received that from the beginning the bony new formation was combined with the fibroma new formation, so regular are the bony formation and the fibroma formation in the entire tumor. Such cases I have observed four times on the upper jaw. The upper jaw formed an entirely solid mass without a maxillary cavity."

CASE 8 (Bellin, reported by Gagnier[2]).—A woman, aged 22, had had a swelling in the right cheek noticed at the age of 14. It was attributed to carious teeth. Almost all the teeth on the right side had been extracted, but the tumor continued to grow.

Physical Examination.—The skin was normal and not edematous. There was a protuberance of the right zygomatic arch and the anterior surface of the entire right upper jaw, so that its normal depressions and elevations were smoothed out. Tender or soft spots were not felt on palpation. The hard palate on the right side bulged downward, most markedly toward the alveolar

1. Hildebrand, quoted by Hippel: Lehrbuch der allgemeinen Chirurgie, 1909, p. 345.

2. Gagnier: Thèse de Paris, 1910.

process. The swelling was of an even, bony hardness throughout. The alveolar process was widened and of the same hardness.

Transillumination from the mouth outward gave total darkness on the right side. The left side was normal. The examination was otherwise negative. The diagnosis was a benign tumor.

Operation.—A partial resection was made. A window was opened into the canine fossa. Directly beneath the cortex was a spongy tissue. The operator removed this tissue piece by piece to a depth of 2 cm., without finding a line of demarcation between it and healthy tissue. Tumor tissue was removed as far down as the periosteum of the hard palate, upward as far as the floor of the orbit. A maxillary cavity was not found. Posteriorly, the clearing was continued as far as possible, and a large opening was made toward the nose. Healing resulted, and had lasted four years when the report was published.

Miscroscopic Examination.—The tumor consisted of bony trabeculae. They were not broad, but had many well developed osteoblasts. These trabeculae were encountered in sections cut in various directions. Between them was well developed connective tissue, chiefly composed of spindle cells with long nuclei. This tissue did not resemble sarcoma tissue; it appeared in places where normally there was marrow tissue. Atypical cells or myeloplaxes were not found.

Case 9 (Cauzard, reported by Gagnier[2]).—A woman, aged 21, had had a painless swelling for ten years in her right cheek. The skin was normal. An even swelling filled the canine fossa, extending upward to the lower orbital border below to the alveolar process in the region of the molars. It was hard, but not tender. The bridge of the nose and the frontal process of the upper jaw were not thickened. The results of examination of the mouth were negative. The alveolar process was thickened on the outer surface. There were carious roots in the place of first two molars. The nose was symmetrical.

Transillumination from mouth outward showed complete darkening of the right upper jaw. A roentgenogram showed marked haziness of the entire body of the superior maxilla. The diagnosis was a paradental cyst. (Diffuse hypertrophy was considered but the suggestion was discarded because the condition was unilateral.)

Operation.—An incision was made in a transition fold from the middle incisor to the wisdom tooth to expose the canine fossa. The walls were markedly thickened, but the maxillary cavity was nonexistent. In its place were masses of spongy bone which permeated the bone without demarcation. The soft tissue was removed without much bleeding, or perforation of the inner wall or opening into the nose. The carious roots were extracted and healing followed.

Microscopic Examination.—Two different kinds of tissue were found in the tumor; the bony trabeculae of normal structure were separated by fibrous tissue, but marrow tissue was not present. Bony trabeculae were formed of ground tissue, in which osteoblasts were regularly recognized. The interstitial tissue was young connective tissue with long cells and small nuclei. Sarcomatous degeneration was not seen.

Case 10 (Hippel).[3]—A boy, aged 11, healthy and from a healthy family, fell four years before he came to the hospital, striking his face against the edge of a table. Some time later, he noticed a swelling in the left cheek which increased slowly and gradually, without pain. About three weeks before examination, it was noticed that the palate had become thick.

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3. Hippel: Ztschr. f. Mund und Kieferchirugie **1**:110, 1915.

Physical Examination.—The skin was normal. There was a swelling of the entire superior maxillary region. The nasolabial fold was obliterated. The swelling was the width of the little finger below the inner angle of the eye, and widened at the left side of the bridge of the nose. It included the mesial two thirds of the zygomatic arch as far as the infra-orbital margin, and extended downward to a line drawn horizontally from the angle of the mouth outward, and lost itself gradually about two fingerbreadths in front of the ear. The skin was freely movable, the surface was smooth, the consistency was bony, without soft spots or parchment crepitation. There was tenderness at only one circumscribed spot over the canine fossa. Irregularities were not present on the lower orbital border; the bulbus did not protrude, and vision was not disturbed. The palate did not divulge on the left side. The upper jaw was evenly swollen from the alveolar process upward beyond the fold of the mucosa, forward almost to the midline and backward over the molar region. The diagnosis was a benign tumor, the nature of which was undecided. A diffuse hypertrophy was thought probable.

Operation.— An incision 4 cm. long was made from the vestibulum oris outward over the tumor, and flat lamellae of tumor tissue were removed for examination. The spongy tissue was found to be soft without a line of demarcation between it and the healthy bone.

Examination of the patient six months later did not show any change. Transillumination from the mouth outward showed the maxillary cavity, cavity of the eye and the pupil on left side to be dark. A roentgenogram made from the occipito-frontal direction showed darkness of the entire superior maxillary bone.

Microscopic Examination.—Irregularly arranged bony trabeculae of various widths were separated by wide, wavy strands of connective tissue. In the fairly homogeneous bony ground substance, some cells were spindle-shaped and some were round. Some had distinct processes. The arrangement of the bone was not lamellary. There were osteoblasts in many places on the margins of trabeculae and osteoclasts in lacunae, more isolated. Connective tissue fibrillae contained numerous cells, mostly spindle-shaped with longish nuclei and isolated round cells, and many distended vessels. There was nothing suggestive of sarcoma. The diagnosis was osteofibroma.

CASE 11 (Uyeno).[4]—A woman, aged 20, who was healthy as a child and came of a healthy family, was troubled with toothache in the upper part of the right jaw at the age of 10. Gradually the right side of the face swelled, without subjective symptoms except occasional toothache.

Physical Examination.—A swelling, the size of a man's fist, was found in the region of the upper part of the right jaw. The angle of the mouth was displaced downward and outward and the right eyeball displaced a little forward and upward. The swelling was caused by a tumor of bony hardness, with a smooth surface. The skin was normal and movable. The swellings extended on to the zygomatic arch, which was thickened in its mesial half, and to the upper lateral limit of that part of the frontal bone which forms the orbit, and gradually lost itself laterally and superiorly. The floor of the orbit bulged upward; the lower orbital border was rounded off and thickened. In the buccal cavity was found, bulging downward, the right half of the hard palate, from which the left molar tooth was missing. It was covered with normal mucous

4. Uyeno: Beitr. z. klin. Chir. **65:** (2); 301, 1909.

membrane. The tumor was of bony consistency throughout, without parchment crepitation. Glandular swellings were not present. The diagnosis was a benign tumor of the upper part of the jaw.

Operation.—All bony connections of the upper part of the jaw were severed, and the bone was removed. It was found that the bony, hard tumor extended far down toward the base of the skull; and here, as well as in the region of the zygomatic arch, many small pieces were chiseled away. Healing was good.

The extirpated tumor measured 9 cm. from top to bottom; the greatest diameter from right to left was 8.5 cm., and anteroposteriorly 7 cm. It weighed 230 Gm. The periosteum was apparently normal. The infraorbital sulcus was indistinct. The demarcation between the alveolar and palatine processes was almost entirely flattened out. The teeth were normal. The tumor was not connected with the roots of the teeth. Toward the nasal wall, the concha nasalis inferior was entirely intact. When the right upper jaw was sawed through, it was found filled by a bony mass, without any cavity. The tumor consisted exclusively of bony substance and was spongy. The tumor was softer than normal bone. On the sawed surface of the entire tumor, blood vessels were recognizable.

Microscopic Examination.—The tumor consisted of bony trabeculae, somewhat narrower than in normal bone, with wider meshes between them. These meshes were filled with finely fibrillated connective tissue, which replaced entirely the marrow substance. In this connective tissue were numerous wide vessels. In many places there was more connective tissue than fibrous marrow; in other places the contrary was true, so that entire portions of the new formation consisted of fibrous tissue alone. Osteoblasts were found around the bony trabeculae. In the bony trabeculae was an entirely bony structure, particularly large, long, star-shaped bone corpuscles and fine canals, but not of lamellary nature. Results in all the preparations taken from various parts, were almost identical. The microscopic diagnosis was osteofibroma.

CASE 12 (Uyeno).[4]—A woman, aged 20, six years before examination, had had a severe inflammation of the throat, with swelling of the left angle of the lower jaw, difficult swallowing and fever, lasting three weeks. Soon afterward a swelling of the left cheek was noticed, increasing slowly without pain. It reached its full size three years before the examination.

Physical Examination.—Swelling of the left half of the face, extending upward to 2 cm. below the under orbital margin, forward as far as the left side of the nose and losing itself gradually behind, was found. If the upper lip was raised, it was seen that the swelling was caused by a tumor on the outer side of the alveolar process of the upper part of the jaw. It began at the left lateral incisor, and extended backward to the last molar tooth. Downward, the tumor extended almost to the teeth, upward to about 2 cm. from the lower orbital margin. It was covered with normal mucous membrane, its surface was almost smooth, its consistency that of bone. The inner side of the alveolar process did not show a swelling.

Operation.—A portion of the tumor was first chiseled off for examination. The chisel struck softer bone tissue of almost even consistency which was fairly well demarcated from the ground tissue. Macroscopically, the tumor looked like an osteosarcoma. A partial resection of the upper jaw was made, and the jaw healed successfully.

Microscopic Examination.—Pieces of tissue from tumor of the antrum of Highmore showed an osteoma richly permeated by fibrous constituents, an osteofibroma.

CASE 13 (Uyeno).[4]—This was a case of pedunculated osteofibroma springing from the alveolar process. A woman, aged 47, had noticed a gradually enlarging tumor of the inner side of the left cheek for two years. One year before examination, the tumor began to grow more rapidly. The teeth on that side had been removed some years before for caries. She had difficulty in swallowing, slight pain, and a hanging of the tongue. The speech and mucosa were normal.

Physical Examination.—The left cheek was somewhat swollen externally. When she laughed a smooth tumor, covered with glistening mucous membrane, appeared in the left angle of the mouth. On the upper alveolar process there was a tumor consisting of three portions; it extended about 5 cm. toward the back and was flattened on the sagittal plane. It was not ulcerated; was not pendulous from a broad pedicle, but hung from the alveolar process, and was movable when touched. The tumor did not involve much of the free surface of the alveolar process, but extended smoothly over the left side of the roof of the mouth a little beyond the midline. Forward, it extended 1 cm. in front of the front teeth; behind, not quite to the end of the hard palate. On the plate of the palate also, the tumor could be moved backward and forward. It was covered with mucous membrane, and it was hard, slightly nodular and insensitive.

Operation.—The tumor was easily pried away from the alveolar process, and removed in toto. It was attached by a narrow pedicle to the outer lamella of the alveolar process and spread out, like a wing, in various directions. After removal of the tumor, the left alveolar process was removed over an extent of 0.5 cm., leaving a bony defect the size of a phalanx of the thumb. In the posterior angle of the antrum of Highmore was a cyst, the size of a pea, filled with mucopurulent material. That was curetted out, care being taken to spare the mucous membrane of the antrum. Healing followed.

Microscopic Examination.—The tumor consisted mostly of wavy strands or irregularly looped fibers of soft connective tissue. There was marked infiltration under the mucosa. In some of these spindle-shaped cells were narrow bony trabeculae. These consisted of different cells; some within the narrow ground substance, were round or oval bone cells with one or two nuclei; others, in the broader ground substance, were star-shaped bone corpuscles. In the margins were also connective tissue cells, which contained much protoplasm. The connective tissue was greater in amount than the tissue of narrow bony trabeculae. Osteoblasts and osteoclasts were not seen. The flat epithelial covering of the roof of the mouth was intact.

CASE 14 (Menzel, Arthur).[5]—A woman, aged 35, had a large tumor of the lower part of the left jaw for twenty-five years. It started, according to the patient, in the region of the lower first molar tooth, and in five years had become twice the size of a man's fist. Twenty years before this examination, Balassa had begun to operate on it, but had been forced to stop because the patient had a dangerous fainting fit. The tumor had grown steadily since then. Ten years before, the patient had begun to limp on the left leg. The family history was negative.

Physical Examination.—The tumor was the size of a child's head, occupied two thirds of the lower jaw, and extended as far down as the cricoid cartilage, where the skin passed over directly on to the tumor.

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5. Menzel, Arthur: Arch. f. klin. Chir. **13**:212, 1872.

The malar bone was forced upward by the tumor. The mouth was drawn out to three times its normal length. From the mouth projected a tumor nodule the size of a fist, on the anterior periphery of which was a tooth and traces of alveolae. The buccal cavity was so filled out by the tumor that the left palate was forced upward for a considerable distance. The posterior border of the ramus extended to the posterior pharyngeal wall, but was not adherent to it. The lower jaw was mobile, but within only slight limits. Two scars traversed the tumor, from the angle of the mouth to the region of the articulation of the jaw, forming an ellipse (scars of old uncompleted operation?). Within the ellipse the skin was entirely immovable, elsewhere it was mobile. The tumor was of firm consistency on the outside, and toward the mouth it was of bony hardness. The diagnosis was a calcified enchondroma.

Operation.—The operation was recognized as dangerous, but was proposed and the patient agreed to it; otherwise the tumor would soon have compromised respiration and the taking of nourishment.

The jaw was sawed through in the region of first molar tooth on right side. Two incisions were made, from the left angle of the mouth over the greatest convexity of the tumor to the articulation of the jaw parallel to those of Balassa, but half an inch farther out. The entire outer surface of the tumor was exposed by dissection of the skin in long strips. The extremity of the jaw which had been sawed was then seized and drawn outward, and the soft parts pushed away.

The insertion of the tendon of the temporalis was four times its normal width and had to be cut. The disarticulation of the joint occurred spontaneously from the weight of the tumor. Hemorrhage was comparatively slight. Spontaneous retraction was expected to shorten the greatly lengthened lower lip. Recovery and healing was good at first. Erysipelas developed in the right cheek one week after operation, and the patient died on the thirteenth day after operation. Autopsy showed that the erysipelas was the sole cause of death.

Description of the Tumor.—The tumor was almost wholly bony. It weighed, after removal of soft parts, more than 3 pounds (1.4 Kg.). The body of the mandible was so increased in height that the ramus was almost completely included in it. The periosteum, which was much thickened on the inner side, peeled off easily. On the outer side, even the skin adhered firmly to the bone by the medium of a hard, white, fibrous mass. The nervus alveolaris inferior, the nervus mentalis and the corresponding canal were unchanged to outward view. The distance through the inframaxillary canal was 24.5 cm. (normal distance, 10 cm.). The nerves were not markedly changed microscopically. A cross-section through the lower jaw, forward through the coronoid process of the mandible and the glenoid fossa, of the temporal bone, showed a hard bony center, surrounded by a layer, varying in thickness and composed of firm, white fibrous tissue, surrounded in turn by the extremely expanded cortical substance of the mandible. The central part was irregular and nodular, composed in the middle of substance resembling that of the diploe and at the periphery of more compact substance.

The fibrous tissue was thickest inferiorly. It filled out all the gaps between the lamellae with tonguelike processes.

The outer bony covering, presumably the expanded mandible, was lacking above, was widest posteriorly and had an outer layer of eburnated substance. In the latter, near the posterior margin of the ramus, was a molar tooth embedded in the bone, the crown downward, one root directed forward, the other back.

A cross-section from the outside inward showed a porous substance, the rather large pores filled with fibrous reddish masses. The fibrous masses were arranged in alveolar fashion like the diploe of the tumor.

Microscopic Examination.—The peripheral fibrous layer and the alveolar nodules both consisted of connective tissue. In the peripheral layer the fibers were mostly fine, straight and in thick bundles. In other places the bundles were thinner and arranged in meshes. In a few places the corpuscles were filled with brown granular pigment over considerable stretches. Isolated among the fibers were single, larger, slightly turbid cells which had large, oval nuclei with sharp contours. The meshes were filled with connective tissue or homogeneous intercellular substance and star-shaped anastomosing corpuscles.

The structure was not markedly different in the central larger soft masses, or in the numerous large and small nodules and veins that traversed the bony mass in all directions. It was also composed of connective tissue which appeared in various forms. Alveolar structure predominated. The fibers were sometimes fine, sometimes thick, and were parallel to each other. In places they were covered with a fine dust, elsewhere they were hyaline and brittle. A lymphadenoid network, sometimes thick, sometimes delicate, was spread between the meshes, and corpuscles were not noticed at points of intersection. This network had a tendency to pick up lime molecules, so that few were found free from it. A finely dusted over membrane seemed to be stretched between the connective tissue trabeculae.

Frequently the margin of the bundles of connective tissue had a homogeneous, light refracting, yellowish border. From this sprang hyaline buds, which sent out other buds, so that some meshes were filled with proliferations resembling a bunch of grapes. Some of the separate "grapes" were loose. Some were composed of many layers and resembled the granules of psammoma.

In some places the alveolar structure gave way to a connective tissue with faintly indicated fibrillation. Occasional stiff fibers took the form of the skeleton of a leaf.

Many deposits of lime, as dust or as larger particles, were in the connective tissue. The hard portion of the tumor, by far the largest part, offered only the picture of normal bone with abundant provision of haversian canals and concentric arrangement of bony layers. There were large numbers of bone corpuscles, usually round, mostly rayed, sometimes with the long rays running exclusively parallel to one another, as in tooth cement. These bone cells were particularly well developed in the diploetic substance. A nucleus was frequently demonstrable in them. In the diploetic substance was reddish marrow, consisting of lymphoid cells; in the larger spaces there were fat globules; in the large ones, particularly in the center of the tumor, were found the soft tumor masses above described.

The tumor was considered an osteoma because the greater part consisted of pure bone tissue, but examination of the inconsiderable soft portion classified it genetically as a fibroma. Calcification and ossification are particularly frequent in tumors of the jaw, though often incomplete and comparatively unimportant. This seems to be the first case reported in which so large a tumor was composed almost wholly of well formed bone. The chief growth of the tumor took place between the second and third molar teeth.

CASE 15 (Mauclaire and Maurel).[6]—The patient was a woman, aged 68, who was admitted to the hospital on Dec. 9, 1912, for an advanced uterine neoplasm. In addition to the uterine lesion, she had a tumor the size of an orange at the angle of the right lower jaw. This tumor was hard and of osseous consistency. It was not adherent to the superficial structures. It was not painful spontaneously or on pressure and was not inflamed. The tumor had developed externally.

The tumor began to grow about twenty years previously following an injury. It grew progressively, and never was painful. All the teeth had erupted normally. A diagnosis of osteoma was made.

She died three weeks after admission. Death was due to the cancer of the uterus. At autopsy, the horizontal branch of the maxilla was resected near the symphysis, and the right half of the lower jaw was disarticulated.

The tumor was rounded; the external surface was convex. It was hard, and was the color of bone. The surface was regular, but there were some elevations and depressions. On the internal surface the alveolar margin was entirely reabsorbed. Above this level the tumor was hollowed out, forming a deep cavity. The internal surface of the cavity was irregular and much less hard. The condyle was rough and irregular, also the coronoid process. The size of the tumor was 7 by 6 by 4 cm.

Histologic examination showed that the tumor was composed of cellular elements with islands of osseous tissue. It resembled a fibroma.

CASE 16 (Monnier, L.).[7]—In a boy, aged 15, in 1911, a tumor began to form on the lower gum a little to the right of the median line. This tumor grew progressively and was painless. In 1912, a temporary fistula formed at the level of one of the lower incisors. The tumor developed uniformly and was not treated except by punctures at various times.

When the patient was admitted to the hospital on October 2, there was a pronounced protrusion of the chin, which was greater on the left side. The overlying skin was healthy.

With the mouth opened, the lower gum seemed to be uniformly swollen but was covered with normal mucosa. The patient did not have any lower incisors or canines.

The tumor was firm, but was more fibrous in its median portion and frankly osseous at the sides. There was one point of softening at the level of the left second incisor where the punctures had been made. The tumor was 6 or 7 cm. long and 3.5 cm. wide. It was absolutely painless on strong pressure. Mastication was possible, except for hard foods.

On October 10, a dentist fitted two rings fixed by bands placed around the lower molars on each side. An operation was performed under general anesthesia on the next day. A horseshoe incision was made extending from the ascending ramus to the other, underneath the inferior border of the jaw. There was abundant hemorrhage. Subperiosteal denudation of the tumor was performed for 10 or 15 mm. along the healthy bone. The mucosa was perforated near the neck of the left molar tooth, a Gigli saw was passed around the bone, and the bone was sectioned. The same operation was performed on the other side, and the body of the maxilla was removed. A prosthetic appliance of aluminum was then inserted and held in place by the rings previously fastened

6. Mauclaire and Maurel: Bull. et mém. Soc. anat. de Paris **88**:113 (Feb. 21) 1913.

7. Monnier, L.: Paris chirurg. **5**:842 (Oct. 24) 1913.

to the molars. This appliance maintained the normal separation of the ends of the maxilla.

The postoperative course was normal, without pain or fever. The sutures were removed on the sixth day, and healing was complete on the ninth day. The scar was scarcely visible.

CASE 17 (Wylie, A.).[8]—A man, aged 53, consulted Dr. Wylie on January 9, complaining of a growth in the palate of twenty-five years' duration. He did not feel any pain and little discomfort; in fact, he said that beyond a certain amount of anxiety it was not troublesome, and, since it had grown slowly and gradually, he had become used to it. Mastication and deglutition were performed without any difficulty, and with the exception of a slight thickness or impaired resonance, his voice and articulation were normal. He had always had perfect health, and his teeth were sound. On examination, a large, smooth, oval swelling was seen occupying the whole of the hard palate. It was the same color as the surrounding mucus; it was not tender to the touch, was firm and slightly movable on steady pressure. Without employing any anesthetic, it was removed by an ordinary polypus snare, and the stump healed rapidly. Dr. Wylie had waited eleven months to see whether there was any recurrence.

Dr. Wyatt Wingrave reports: "The tumor has the appearance of a new potato; it measures 5 to 2.8 cm. and weighs 13 Gm. The cortical part, for a depth of about 5 mm. is firm and tough, and encloses a hard, stony core, which reaches the surface at its point of attachment. In structure, the cortex is composed of densely packed white fibers mingled with elongated fusiform cells (fibroblasts). The stonelike core consists of compact bone with relatively small cancellous spaces, resembling ivory or petrous bone. It is evidently an osteoma growing from the periosteum of the maxilla, to which it was attached. There is no sign of any sarcomatous tendency."

COMMENT

The three cases that I have reported, together with those collected from the literature, comprise a group of seventeen cases in all. In reviewing this small group, the four cases spoken of by Hildebrand must be omitted on account of lack of details about them.

Many of these tumors begin in childhood, although the patient may not apply for treatment until adult life. Hippel says that they start between the ages of 7 and 14. In eight cases in this series, the onset was in youth, but in five cases it was well on into adult life. The most advanced age of onset was 54; the youngest was 7.

It is difficult to say much about the influence of sex, as eight of these patients were women and five were men. There was a previous history of carious teeth or an inflammation about the jaw in five cases. In two other cases the patient gave a history of an injury of the face previous to the appearance of the tumor.

The symptomatology of these tumors is that of a slow growing, painless tumor that involves either the upper or the lower jaw. By its size or position it may interfere with the action of the jaws, but the nasal

8. Wylie, A.: J. Laryngol. Rhinol. & Otol. **24**:30 (Jan.) 1909.

cavity is usually not encroached on. The tumor is a firm, smooth mass that is not tender, even to firm pressure. It is closely attached to the bone, but the overlying skin or mucous membrane is free and unchanged. Macroscopically, this kind of tumor is usually soft and homogeneous, with a moderately good blood supply. The tumor has no capsule, but is definitely demarcated from the bone. The bed of the tumor appears as smooth, unchanged bone. The tissue of the tumor has much the appearance and friability of that of a sarcoma. In those cases in which there is more definite bone formation, the tumor may show hard areas of bone associated with the fibroma tissue. In some instances, the bone may enclose the fibrous portion as a soft center in a bony mass, or the fibrous tissue may be external surrounding the bone formation in the center. The tumor is not connected with the roots of the tooth in any way.

Microscopically, according to Hippel and Uyeno, the tumor is characterized by the simultaneous growth of bone and connective tissue from the start. Judged by that characteristic, the cases of Menzel, Monnier, Wylie and the third case of Uyeno could not be included in this collection, which would leave only thirteen cases of definite osteofibroma.

In these undoubted cases, the microscope shows trabeculae and islands of bone tissue separated by strands of connective tissue instead of marrow. The bony trabeculae are irregular and of varying widths, and osteoblasts are frequently seen. Marrow formation does not appear, and there is not a lamellary arrangement of the bone cells. The interstitial tissue is composed of many strands of young connective tissue cells which are spindle shaped with elongated nuclei. The sections do not show evidence of sarcoma tissue at any place. Numerous distended vessels are scattered through the tumor tissue.

The four doubtful cases show the same connective tissue formation, but the bone appears as a more definite mass and shows a lamellary arrangement. In these cases the tumor is more probably a fibroma which has undergone ossification in part.

Osteofibromas do not have a capsule and do not show evidence of growth from, or attachment to, the periosteum. They are evidently endosteal tumors.

Clinically, it is difficult to differentiate these tumors from central fibromas, endosteal osteomas and chondromas. Hippel says that the principal difference in the upper jaw is that osteofibromas do not tend to narrow the nose, and that they cause slight displacement. Odontoid cysts and fibrocystic disease of the jaw can be recognized usually by the roentgenograms. Diffuse hypertrophy and leontiasis ossea affect more than one bone.

Microscopically, differentiation is easy except in the case of leontiasis ossea. Hippel says that Bordenhauer's description of his case of leontiasis ossea agrees exactly with the histology of osteofibromas. Only the clinical picture can differentiate the two processes.

The prognosis is generally favorable. These tumors are benign, and do not tend to recur after thorough removal. They grow slowly, and it is not known whether they ever reach a spontaneous standstill.

The only treatment advisable is a complete surgical removal of the tumor. In most instances a line of demarcation can be found, and the tumor can be enucleated or curetted out. Resection of the bone is not necessary, except in the case of extensive growths. For the extensive tumors, a preliminary ligation of the external carotid artery will be of material aid in simplifying the technic.

THE RELATIONSHIP OF CHRONIC SUBDURAL HEMATOMA AND PACHYMENINGITIS HEMORRHAGICA INTERNA

A REPORT OF EIGHT CASES, WITH THE REPORT OF FINDING BILE PIGMENT IN THE HEMATOMA *

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Chronic subdural hematoma as a definite clinical and pathologic entity is only of recent prominence. Particularly is this true of cases which result from trauma. Putnam and Cushing [1] recently reported twelve cases, contributed by members of the Society of Neurological Surgeons, placing special emphasis on the traumatic features, with a comprehensive review of the literature. Within a period of five months, four cases of this condition have come to necropsy at this hospital. In three of these there was a definite relationship to trauma. Four more cases have been added from pathologic records.

REPORT OF CASES

CASE 1.—*Traumatic subdural hematoma of two months' duration with psychosis.*

C. S., an American laborer, aged 46, was admitted to the hospital on April 29, 1926, eleven hours after he had been picked up on the street in a semicomatose condition. Dispensary records state that he had been struck by an automobile eight weeks before, sustaining a laceration of the left frontal region. Consciousness was not lost, and there was neither clinical nor roentgen-ray evidence of fracture. Ten days after he was injured the wound in the scalp had healed, but he complained of a dull headache of two days' duration with occasional vertigo. There was nothing in the physical examination at this time to account for these symptoms. The patient was referred to the medical dispensary for special tests and observation. He failed to report, and was not seen until he was admitted in a state of coma. Relatives said that he had been a heavy drinker for five years, especially after he was injured. Headache had been constant since one week after he received the injury. About five weeks after injury, signs of psychosis appeared, and were pronounced five days before admission.

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1. Putnam, Tracy Jackson, and Cushing, Harvey: Chronic Subdural Hematoma, Arch. Surg. **11**:229 (Sept.) 1925.

On admission he was in a comatose condition, but had good color. There was a scar in the left frontal region. The blood pressure was, systolic, 120; diastolic, 80, and the pulse rate was 90. There was a lateral nystagmus of both eyes, but otherwise the cranial nerves were apparently normal. Breathing was abdominal. The pectoral muscles and the right upper extremity were spastic, with increased reflexes. The epigastric and cremasteric reflexes were normal. Patellar reflexes were exaggerated on both sides. He did not show abnormal sensory signs. The spinal fluid was clear, under normal pressure and contained 2 cells per cubic millimeter, without any increase of globulin. The result of the Wassermann test was negative. The coma became deeper three

Fig. 1.—Inner surface of the dura in case 1, showing membrane covering left hemisphere.

days after admission, and signs of pulmonary congestion appeared. Death occurred two days later.

Autopsy.—The dura was unusually adherent to the skull, especially over the left parietal region, where it was brownish red and appeared thickened. The inner surface of the dura on this side was covered with a layer of dark reddish brown, organizing blood clot which extended over almost the whole of the left hemisphere (fig. 1). The average thickness near the center of the clot was 4 mm., and it became gradually thinner toward the margins. The inner surface of the clot was a thin, glistening, semitransparent membrane, apparently

continuous with the inner surface of the dura at the edges. The clot was easily split into three layers; a thin, fibrous inner layer, a thick middle layer of friable clot and a thin, firm outer layer closely attached to the dura. The arachnoid beneath the clot was unbroken and of normal appearance. Cerebral convolutions were not flattened or discolored. The skull was not fractured.

The dura was of normal thickness, and attached to it was a layer of dense fibrous tissue containing many capillaries and large spaces lined with endothelium. Some of the spaces contained blood, but many were empty. This fibrous tissue was infiltrated with endothelial leukocytes, many containing blood pigment. Arising from this layer was a network of capillaries and fibroblasts organizing the central area of old hemorrhage (fig. 2). Here were many

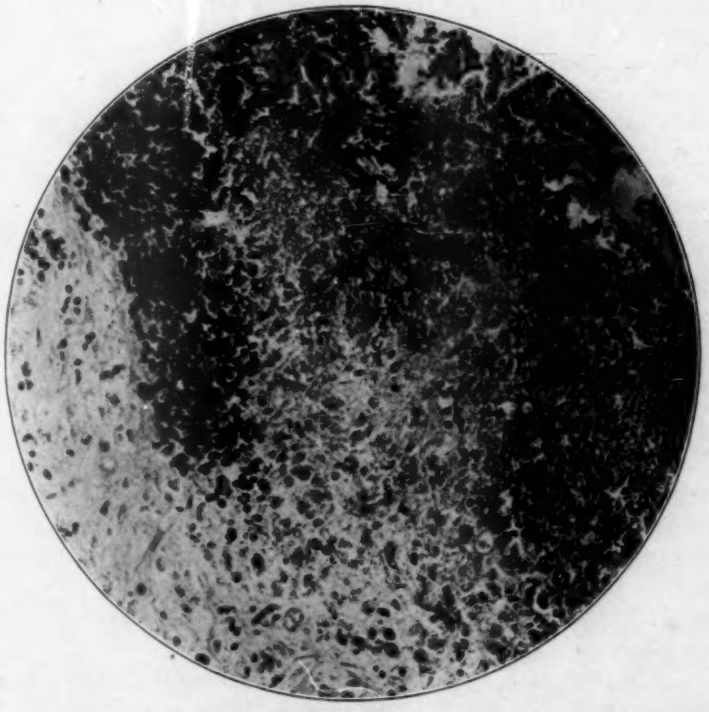

Fig. 2.—Fibroblasts and capillaries invading and organizing clot. × 210.

brownish crystals mostly contained in endothelial leukocytes. The inner membrane was a comparatively thin layer of dense fibrous tissue limited on its inner side by scattered endothelial cells. This tissue also contained many endothelial leukocytes filled with pigment.

Other anatomic observations were terminal lobular pneumonia, chronic pulmonary tuberculosis, urethral stricture and chronic cystitis.

CASE 2.—*Traumatic subdural hematoma of two weeks' duration.*

E. E., a white woman, aged 68, was first admitted to the hospital on June 27, 1926. She was intoxicated, and had a hematoma of the left frontal region of the scalp caused by a fall. Roentgen-ray and clinical tests did not show a fracture of the skull. Twelve hours after entrance she left the hospital

against advice, saying that she felt well. Nine days later she became irrational, and was readmitted to the hospital. Neighbors said that she had changed considerably since she was injured, and had been despondent for about five days.

There were ecchymoses about the left frontal region and the left eye, a systolic murmur at the apex and contracture of the toes of the right foot. The lower portion of the left seventh cranial nerve was slightly weak, and the tongue protruded to the left. The patellar reflex was increased on the left. The pulse rate was 105, the temperature 99.4 F. and the respiration 40. The blood pressure was, systolic, 180 and diastolic, 105. The spinal fluid was slightly xanthochromic, under normal pressure and did not contain an increase of cells or globulin. The result of a Wassermann test of the spinal fluid was negative. A second roentgen-ray examination at this time showed that the skull was not fractured. The patient's condition remained unchanged until death four days later.

Necropsy was limited to the head. The pupils were equal and regular, 4 mm. in diameter. There was a hematoma of the scalp 2 cm. in diameter above the outer angle of the left eye, and there were ecchymoses about the left eye and in the left submaxillary region. Beneath the dura on the right was a dark red blood clot apparently beginning to organize. This clot extended from the base in the middle fossa to the vertex and about 4 cm. anteriorly and posteriorly from the middle branch of the middle meningeal artery. There was a small amount of blood in the right subarachnoid space, although the arachnoid was not injured. The cortex beneath the clot had a slight yellowish tinge. The skull was not fractured. The comparatively recent clot beneath the dura was undergoing organization in the portion next to the dura. Granulation tissue in the organizing clot contained many leukocytes, mostly endothelial, filled with red blood corpuscles and blood pigment. There were many capillaries and large spaces lined with endothelium. Some of these spaces contained blood. The piamater was infiltrated with leukocytes, mostly endothelial, filled with blood pigment, but also many lymphocytes. The lumen of one artery in the pia contained a mass of firm, fibrous tissue almost obliterating the lumen. Van den Bergh tests on the liquid portion of the clot did not show an increase of bilirubin over that of blood from the heart.

CASE 3.—*Traumatic subdural hematoma of two months' duration with recurrence of symptoms.*

B. H. C., a white man, aged 54, was first admitted to the hospital in a semicomatose condition on May 31, 1926. About two weeks previously he had struck his left frontal region against an open door. He was unconscious for a time, and afterward complained of constant, dull headache and general weakness. This continued until the day of admission, when he was found in a stupor.

The pupils were equal and regular, reacting normally. The result of the ophthalmoscopic examination was negative, and the cranial nerves did not show disturbance. Contractures, spasms or paralysis were not present. Biceps and patellar reflexes were active, especially on the right side. Abdominal reflexes were not elicited. Both achilles' tendons were active, and there were suggestive Babinski and Oppenheim signs on both sides. Temperature, pulse and respiration were normal. The blood pressure was 170 systolic and 90 diastolic. The spinal fluid was clear and under normal pressure. The amount of globulin was not increased. There were 6 cells per cubic millimeter of fluid. Results of a Wassermann test were negative. The patient's mental condition gradually

improved, and he was discharged two weeks after entrance, with apparently complete recovery.

The patient remained well until July 11, 1926, two months after the original injury, when he complained of a violent headache. The next morning he was admitted in a semicomatose condition and was irrational. Reflexes on the right side were hyperactive. The coma gradually deepened, and death occurred six days after the patient was admitted.

At autopsy external evidence of injury was not found. Attached to the inner surface of the dura, covering practically the entire left hemisphere, was a partially organized blood clot, the exterior of which was olive green and fairly firm, while the interior was dark red and soft (fig. 3). The inner surface of

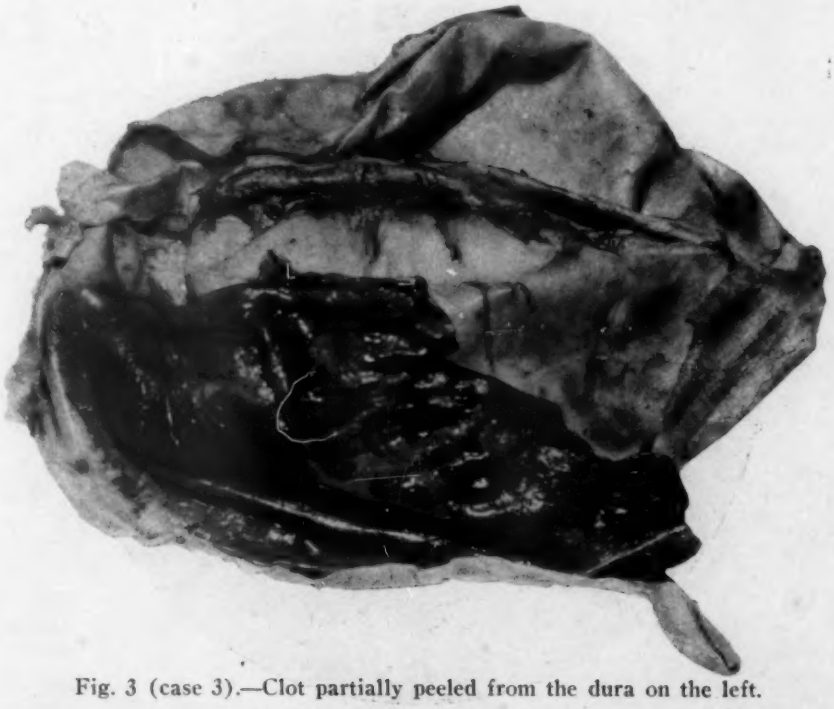

Fig. 3 (case 3).—Clot partially peeled from the dura on the left.

this clot was a thin, glistening, semitransparent membrane, apparently continuous with the inner surface of the dura, although it was easily stripped off. The convolutions of the left cerebral hemisphere were distinctly flattened. The arachnoid and the cortex beneath the clot were a faint greenish brown. The skull was not fractured.

There was a layer of fairly loose fibrous tissue moderately infiltrated with lymphocytes, and pigmented endothelial leukocytes, beneath the dura. In this tissue were many capillaries and large spaces lined with endothelium (fig. 4). Arising from this layer was a network of capillaries and fibroblasts invading an old blood clot. The inner membrane was a thin layer of dense fibrous tissue with scattered endothelial cells on the side next to the arachnoid. The piamater was thickened and infiltrated with lymphocytes and endothelial leukocytes filled with blood pigment. In one section these pigment-laden endothelial

leukocytes were found in the outer portions of the cortex. The van den Bergh test applied to the liquid portion of the clot showed six units of bilirubin. Control of the serum from the blood of the heart showed 0.2 units.

Other anatomic observations were pulmonary congestion, chronic splenitis and healed perihepatitis.

CASE 4.—*Subdural hematoma without history of trauma.* J. C., a negro, aged about 40, was admitted to the hospital on Aug. 15, 1926, unable to talk. There was weakness of the entire right side. He had complained of persistent, dull headaches for some time, but had been well otherwise until three days before he was admitted. Relatives said that he was a heavy drinker, but a history of injury to the head could not be obtained.

Fig. 4.—Large spaces lined with endothlium in loose fibrous tissue just beneath the dura. The irregular formation of the endothelium may be seen. × 210.

The lower portion of the left seventh cranial nerve (supranuclear) was weak. The tongue protruded to the left. The right arm and leg were decidedly weaker than the left, but did not twitch or jerk as did the left arm and left pectoral muscle. Tendon reflexes were hyperactive on the right. There were Babinski and Oppenheim signs and ankle-clonus on the right. The spinal fluid was clear and under normal pressure. The amount of globulin was not increased. There were 50 mononuclears per cubic millimeter. The result of the Wassermann test was negative. Three days after admission the patient was able to mutter a few words, and weakness on the right side was less pronounced, but death occurred the following day.

At necropsy a partially organized subdural clot was found, 10 mm. thick, covering almost all of the left hemisphere. The inner surface of the clot was a thin, greenish brown, glistening membrane, while the middle was composed of a soft, dark red clot. There was a thin, fibrous outer layer attached to the dura. Convolutions beneath the clot were flattened, but the arachnoid and the cortex were of normal color. Beneath the dura was a layer of loose fibrous tissue containing capillaries and large spaces lined with endothelium. Many of these spaces were filled with blood. This tissue was infiltrated with lymphocytes and endothelial leukocytes. Most of the latter contained blood pigment. In some places were large collections of lymphocytes and endothelial leukocytes. Beneath this layer was an old blood clot undergoing organization. The inner

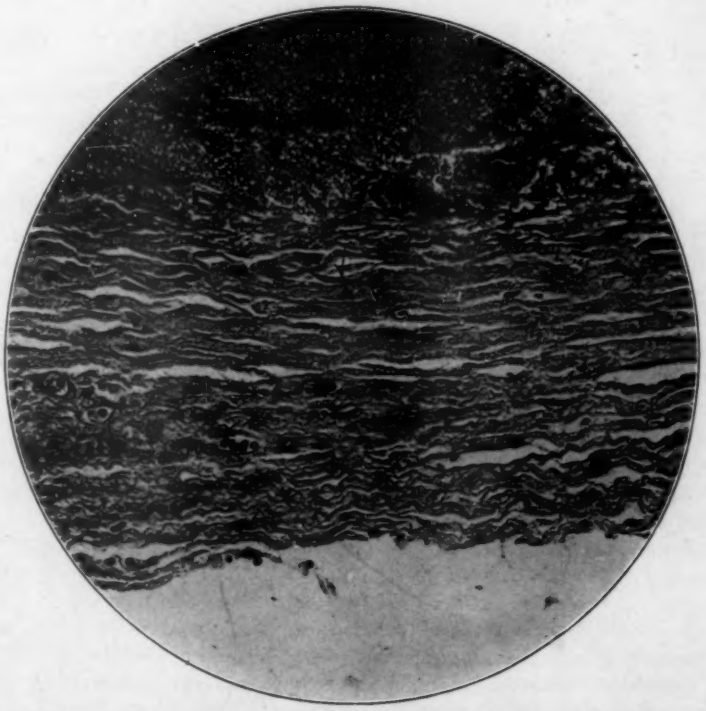

Fig. 5.—The inner fibrous membrane of the clot, showing endothelium on the free surface; × 210.

membrane was a thin layer of dense fibrous tissue covered with scattered endothelial cells on the side next to the arachnoid (fig. 5). A van den Bergh test of the liquid portion of the clot showed 4 units of bilirubin. Control on blood from the heart showed 0.2 units.

Other observations were terminal congestion of the lungs, liver and spleen, slight chronic nephritis and slight chronic pancreatitis.

In a review of the last 1,900 necropsies in this hospital, only the following four cases were found diagnosed as chronic pachymeningitis hemorrhagica interna. History of trauma was not elicited in these cases.

CASE 5.—*Pachymeningitis hemorrhagica interna.*

S. M. B., a white man, was admitted to the hospital, unconscious, Feb. 1, 1915. He had been a rather heavy drinker for ten years. About a month before admission he began to have severe headaches. Two weeks later he lost consciousness for about two hours. At this time his speech was unintelligible, but paralysis was not noticed. The day before admission he fell and lost consciousness; during the night general flaccid paralysis of the upper and lower extremities developed. On admission the right pupil was dilated and fixed, the left pupil contracted and fixed. There was a slightly choked disk. Both arms were flaccid, especially the left. Patellar and elbow reflexes were absent. The Babinski sign was positive. He showed Cheyne-Stokes respiration, and there were moist râles over both lung fields posteriorly. Death occurred nine hours after admission.

At necropsy the left cerebral hemisphere was covered with clot, and on the left, anterior to the fissure of rolando was similar material mixed with thin, grayish fluid. The cortex beneath these areas was slightly depressed. The inner surface of the dura was covered with similar grayish membrane which stripped easily from the layer of clot beneath. Beneath the dura was a layer of rather loose fibrous tissue which was infiltrated with leukocytes, including endothelial cells, filled with blood pigment, lymphocytes and a few polymorphonuclears. This tissue contained numerous capillaries and large spaces lined with endothelium, some containing blood. In and beneath this layer were large areas of old hemorrhage undergoing organization. Sections of the cortex beneath the clot showed thickened and congested piamater and arachnoid with marked reaction of polymorphonuclear leukocytes, lymphocytes and pigmented endothelial leukocytes.

CASE 6.—*Pachymeningitis hemorrhagica interna.*

E. T., a colored man, aged 75, was admitted to the hospital on Nov. 17, 1916. The history was not obtainable. The patient was unconscious and cyanotic, and the respiration was labored. Sounds of the heart were not audible, nor was the radial pulse palpable. The pulse rate (abdominal aorta) was 68. The pupils were dilated, but ten minutes later contracted. They did not react to light. Reflexes were absent. The percussion note was dull over the posterior portions of both lungs. The patient died two hours after admission.

At autopsy the inner surface of the dura over the left hemisphere was covered with a dusky red, soft, glistening membrane which could not be peeled off. There were a few small, similar areas on the right, posteriorly. Convolutions beneath the membrane appeared dull and slightly flattened. Beneath the dura was a thin layer of dense fibrous tissue containing elongated, endothelial-lined spaces, some filled with blood. Pigmented endothelial leukocytes were fairly abundant. Fibrous strans from this layer invaded a layer of old blood clot, but there was little active organization, many lakes of clot being encapsulated by dense fibrous tissue. The inner layer was a thin membrane of dense fibrous tissue lined with endothelium. Other pathologic observations were: lobular pneumonia, chronic myocarditis and chronic nephritis.

CASE 8.—*Pachymeningitis hemorrhagica interna.*

C. B., a colored man, aged 55, was first admitted to the hospital on Aug. 17, 1918. He had used considerable liquor until two years before admission. The complaint was precordial pain. The reaction to the Wassermann test was ++++. A diagnosis of aneurysm of the descending arch was made. He was discharged on September 22, but was readmitted on Jan. 12, 1919. Further

history was not obtainable at this time. Dyspnea was marked. The pupils were equal and reacted to light and accommodation. The physical signs in addition to aneurysm, were those of pneumonia, but the temperature was only from 96 to 99 F., with a pulse rate of from 88 to 120, and respiration from 20 to 48. He was delirious, noisy, and caused much disturbance. Death occurred two weeks after admission.

At necropsy there was a pinkish-yellow, smooth sheet beneath the dura, free from the arachnoid and easily peeled from the dura. It covered the greater portion of the right hemisphere, and was about the consistency of a piece of thin, wet leather, though not so tough. The subarachnoid space contained an excess of clear fluid. Beneath the dura was a layer of fairly dense fibrous tissue infiltrated with numerous pigmented endothelial leukocytes and some lymphocytes. Capillaries were numerous in this tissue, as were large, flat spaces lined with endothelium. Capillaries and fibroblasts springing from this layer were invading an old blood clot, which was limited internally by a thin fibrous membrane.

Other observations were: lobar pneumonia, and dilatation of the arch of the aorta and the innominate artery.

COMMENT

The source of the original hemorrhage in these cases is not clear. Suffice it to say, that following cranial trauma, often slight, possibly with some predisposing vascular lesion, there is bleeding from a small vessel of the dura or from one of the veins entering the sinuses. This may be a single large hemorrhage, repeated small hemorrhages or slow, constant oozing. The relation of the hemorrhage to the middle meningeal artery in the patient in case 2 suggests rupture of a branch of this vessel.

Reaction to the hemorrhage follows approximately the same course as in extravasation of blood elsewhere; namely, reaction of leukocytes and fibroblasts with consequent organization. The inner membrane is formed by growth of fibroblasts and endothelium from the dura at the edges over the bridge formed by the clot. The exception in these cases is the formation of spaces lined with endothelium in the organizing tissue just beneath the dura. It is probable that these spaces are formed by the proliferation of detached bits of dura endothelium in the clot, forming cystlike structures, as may occur on other serous or epithelial surfaces. Many of these spaces contain blood, and in some sections they may be seen to connect with capillaries. This connection may occur by fusing, during the simultaneous formation of these spaces and the capillaries growing into the clot, when cellular proliferation is active. The occurrence of repeated hemorrhages with recurrence of symptoms may be explained by rupture of these blood-filled spaces during sudden changes of pressure, as in coughing or straining. In our cases definite histologic evidence of repeated hemorrhage was not evident, though in some portions of the old clots the blood cells were remarkably well preserved, and in case 3 there was recurrence of symptoms.

There were no histologic differences between the cases with history of trauma, and those in which such history was not elicited. In the recent, actively organizing clots the endothelial cells lining the cystic spaces were more scattered and irregular, capillaries were more numerous, and fibrous tissue was looser than in the older and more fully organized clots (fig. 6). In general, the clots in cases without a history of trauma appeared older and more nearly healed. However, the patients in cases 1 and 3, with definite relationship to trauma, had older and better organized fibrous tissue and endothelium than those in

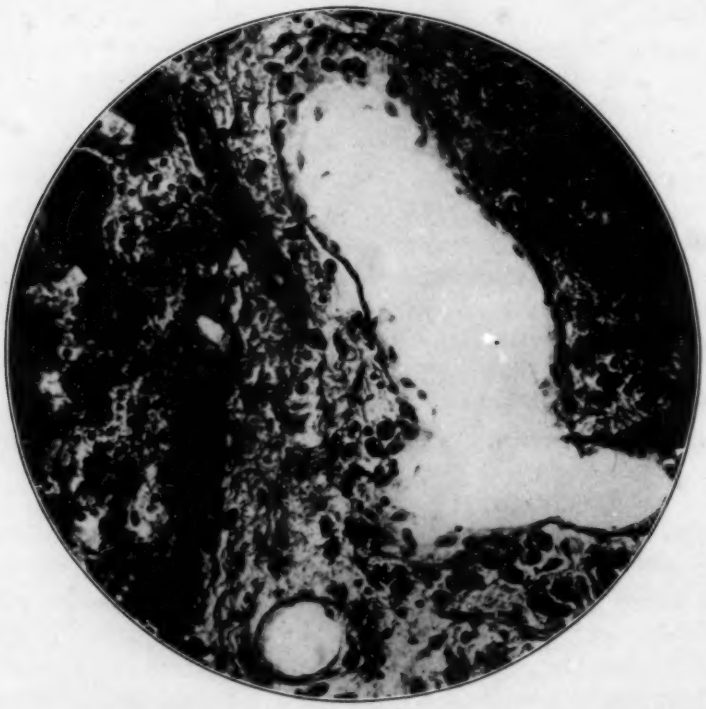

Fig. 6.—Empty space lined with endothelium in case 6. Fibrous tissue is dense and well organized. Endothelium is well developed and regular. Some endothelial cells seen on the flat appear plump; ×210.

cases 4 and 5, in which there was not a history of trauma. We believe that features, such as development of endothelium, which are usually considered as differentiating chronic subdural hematoma and chronic pachymeningitis hemorrhagica interna, are rather differences in degree of organization than differences in type.

The high concentration of bilirubin in two of these clots (thirty and twenty times that in the blood from the heart) and crystals of hematoidin in others indicates that bile pigment is formed during their

absorption and organization. Van den Bergh, quoted by Wells,[2] also found bile pigment in a case of subdural hematoma in a concentration corresponding to that in bile from a fistula of the gallbladder. These facts are of interest in connection with the work of Mann [3] and Whipple [4] and their associates on the extrahepatic origin of bile pigment.

Cushing [1] has suggested that the mesothelial cells of the leptomeninges are similar if not identical with the cells of the reticuloendothelial system, which have come into prominence as the most probable site of origin of bile pigment.[5] These cells have in common the ability to phagocytize red blood cells, colloidal metallic solutions and finely divided solids.[6] Essick [7] and Weed [8] have shown that the cells of the outer and inner layers of the arachnoid, under the stimulus of particulate matter, enlarge, become phagocytic for red blood corpuscles, carbon and cinnabar granules, and multiply, some becoming under appropriate conditions freely moving macrophages in the subarachnoid space. Rich [5] says that the meninges appear to be an exceptionally favorable site for the crystallization of the bile pigment within living cells. These characteristics—taking up particulate matter and red blood corpuscles, becoming free phagocytes and the formation of bile pigment —indicate that the cells of the lining of the meninges are potential, if not normal, members of the reticulo-endothelial system, and as such are concerned in the formation of bile pigment, at least under pathologic conditions.

The factors of alcoholism and insanity which accompany so many of the cases of pachymeningitis hemorrhagica reported must be taken into account in evaluating the apparent absence of injury. Alcoholism was prominent in five cases in this series, and contributed to the trauma in two. The drunkard with contusion of the scalp who does not remember receiving an injury is not uncommon. Psychosis appearing in so many of the known traumatic cases explains the frequent occurrence of pachymeningitis hemorrhagica at necropsy in asylums, since the

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2. Wells, H. G.: Chemical Pathology, Philadelphia, W. B. Saunders Company, 1925, p. 540.

3. Mann, F. C.; Bollmann, J. L., and Magath, T. B.: Studies onthe Physiology of the Liver, Am. J. Physiol. **69**:393, 1924.

4. Whipple, G. H., and Hooper, C. W.: Icterus, J. Exper. Med. **17**:612, 1913.

5. Rich, A. R.: The Formation of Bile Pigment, Physiol. Rev. **5**:182, 1925.

6. Addis, T.: A Working Hypothesis of Hemoglobin Pigment Metabolism, Arch. Int. Med. **15**:413 (March) 1915.

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8. Weed, L. H.: The Cells of the Arachnoid, Bull. John Hopkins Hosp. **31**:343, 1920.

mental derangement is a result rather than a cause of chronic subdural hematoma. The degree of trauma necessary to produce this lesion, not sufficient to cause fracture in any case in this series, may be so slight that it requires special effort on the part of the examiner and the patient to obtain a history of injury. In the old case in the alcoholic patient and in the insane person it is especially difficult to get such information. It is probable that most, if not all, cases, of so-called spontaneous pachymeningitis hemorrhagica have a beginning in a forgotten injury.

Symptoms of chronic subdural hematoma as presented by Putnam [1] fall into two classes: first, those due to general increase in intracranial pressure, as headache, vertigo, vomiting, slow pulse and choked disk; second, those due to local disturbances, as paralysis, sensory disturbances (rare), convulsions and aphasia. In addition, there may be those of meningeal irritation, as stiff neck. These signs may occur in almost any combination, and, besides being variable and fleeting, are likely to be atypical and incomplete. In this series a latent period, of varying length, was the rule. Headache followed by vertigo, vomiting, psychosis and coma is the common course. Choked disk was not found in the four cases recently observed, and was indefinite in case 5. It is often surprising that there are so few physical observations. Terminal lobular pneumonia is common. Increased reflexes, spasticity of various muscle groups and disturbances of the third and fourth cranial nerves are the chief neurologic observations. The spinal fluid is usually normal in all respects, though it may be xanthochromic, or it may contain blood in those cases in which the arachnoid is injured. The temperature varies little from normal, though it is usually slightly subnormal toward the end. The pulse is often a pressure pulse.

Diagnosis depends on a history of cranial trauma, often slight, followed by a variable latent period. It may be impossible to elicit history of injury. Following this is a period of headaches, continuous or intermittent, increasing in severity, then psychosis, coma and death. If the diagnosis is made early and surgical treatment instituted, the prognosis is fairly good.[1]

CONCLUSIONS

1. Chronic subdural hematoma and pachymeningitis hemorrhagica interna are the same, clinically and pathologically.

2. Both probably have their origin in trauma, with some predisposing vascular lesion as a factor.

3. Trauma, headache, psychosis and coma is the usual sequence with additional variable neurologic signs.

4. This condition should be considered in patients presenting this series of symptoms, and surgical treatment instituted if indicated.

5. The lining cells of the meninges are probably potential members of the reticulo-endothelial system.

INFLUENCE OF THE LIVER ON TOXICITY OF BILE *

EDWARD C. DAVIDSON, M.D.
AND
WILLIAM C. EMERSON, M.D.
DETROIT

The fact that bile peritonitis is highly fatal has long been recognized by surgeons. It has been demonstrated repeatedly that bile injected intravenously or intraperitoneally into animals is toxic. The first extensive study of this subject was made by von Dusch [1] in 1854. Since that time many valuable contributions have been made, but a great deal of the pathology remains unexplained.

Bunting and Brown [2] either cut the gallbladder of rabbits and allowed the bile to escape into the peritoneal cavity or injected intraperitoneally from 0.25 to 0.5 cc. of bile per kilogram of body weight. Death occurred in less than twenty-four hours and was attributed to direct action on the myocardium, which revealed degenerative changes. The local pathologic effects which were observed may be summarized in the statement that bile produced necrosis of every type of tissue with which it came in contact. This work was repeated by Frothingham and Minot,[3] who found bovine bile less toxic for rabbits than bile of their own species.

Meltzer and Salant [4] showed that when a few cubic centimeters of ox bile was given rapidly to a rabbit intravenously, the animal died almost immediately in convulsions, while, when given slowly, as much as 50 cc. of a 50 per cent solution was tolerated. They concluded that the confusion in the literature about the relative toxicity of bile depended entirely on varied speed of injection.

The effect of intravenous injection of pig bile and its various constituents on the circulation was investigated by King and Stewart.[5] They observed a slight preliminary rise of blood pressure with whole bile and a secondary continuous fall until death occurred. As the blood

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* From the Surgical Service of the Henry Ford Hospital.

1. Von Dusch, T.: Habilitationschrift, Leipzig, 1854.

2. Bunting, C. H., and Brown, W. H.: The Pathology of Intraperitoneal Bile Injections in the Rabbit, J. Exper. Med. **14**:445, 1911.

3. Frothingham, C., and Minot, G. R.: The Effect of Injection of Bovine Bile into Rabbits, J. M. Research **27**:79, 1912.

4. Meltzer, S. J., and Salant, W.: Studies on the Toxicity of Bile, J. Exper. Med. **7**:280, 1905.

5. King, J. H., and Stewart, H. A.: Effect of the Injection of Bile on the Circulation, J. Exper. Med. **11**:673, 1909.

pressure decreased, a bradycardia developed which was later replaced by an arrhythmia. These effects were eliminated either by division of the vagi or by the administration of atropine. They next prepared bile salt of biliverdin was found to be nontoxic. As a 20 per cent increase the latter reproduced the results obtained with whole bile. The calcium salt of biliverdin was found to be nontoxic. As a 20 per cent increase in the calcium of the blood was observed during the experiments, it was concluded that calcium was protective against toxic bile pigment.

The conclusion attributing the toxicity of bile to the pigment is difficult to reconcile with certain known facts. In early obstructive jaundice and in rapidly occurring hemolytic anemias there may be a great accumulation of pigment in the tissues and plasma without any of the symptoms of bile toxemia. On the other hand, bile peritonitis clinically and in experimental animals may be lethal before even the sclerae are tinged with bile. Were the toxicity of bile due to pigment alone and the lack of symptoms in jaundice due to the pigment being combined with calcium, then there should be a parallelism between the calcium of the blood, the van den Bergh reaction of the blood and the symptomatology. This has not been observed. In obstructive jaundice there is a large output of bile pigment in the urine without a similar rise of the calcium, however the output of calcium in the feces is increased.[6] This necessitates the conclusion that there is considerable toxic uncombined pigment constantly in the circulation or that the kidneys have the power of splitting the calcium from the calcium pigment molecule. Such a function of the kidney has not been demonstrated.

It would seem, therefore, that in obstructive jaundice the bile in the blood stream may be detoxified by some organ, or there may be a depression of the function of the liver, and all the normal elements of bile may not be escaping into the circulation. With this conception, in view of the work of Mann,[7] Rich [8] and others concerning the extrahepatic formation of bile pigment, the degree of deposition of pigment would not necessarily be an index of the toxemia. This is nearer in accord with the clinical facts.

DETOXIFYING ACTIVITY OF THE LIVER

There is a great deal of evidence showing that the liver is capable of destroying certain soluble toxic substances. Buys [9] incubated emulsions

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6. King, J. H.; Bigelow, J. E., and Pearce, L.: Experimental Obstructive Jaundice, J. Exper. Med. **14**:59, 1911.

7. Mann, F. C.: Sheard, C.: Bollman, J. L., and Baldes, J.: The Site of the Formation of Bilirubin, Am. J. Physiol. **74**:497 (Nov.) 1925.

8. Rich, A. R.: On the Extrahepatic Formation of Bile Pigment, Bull. Johns Hopkins Hosp. **36**:233 (April) 1925.

9. Buys, E.: Contribution à l'étude de l'action déstructive exercée par le foie sur certains alcaloides, Ann. Soc. Roy. d. sc. méd. et nat. de Bruxelles **4**:73, 1895.

of frog and rabbit liver with hyoscyamine and found that it was completely destroyed. Cloelta [10] performed similar experiments with a tropine and found that rabbit liver destroyed it. Dixon and Lee [11] and Edmunds and Smith [12] demonstrated that the livers of both normal and tolerant animals possessed some power of destroying nicotine. Weiss and Hatcher,[13] discussing the destruction of drugs, state that atropine, morphine and strychnine are partially broken down in the body, that this is due to fermentation and that the liver is the organ usually chiefly responsible.

It has been shown by Falls [14] that in sensitized animals the liver may modify the effect of the protein used to produce sensitization. He found that from 0.3 to 0.5 cc. injected into the jugular vein of a sensitized guinea-pig caused death within from three to five minutes, whereas from 0.8 to 1.5 cc. was required to produce death in from twenty to thirty minutes when injection was made into a mesenteric vein. The experiments of Manwaring and Crowe [15] indicate that the liver of a sensitized animal may destroy the toxicity of foreign protein. They observed that when a mixture of foreign protein used for sensitization of guinea-pigs, together with blood of a sensitized animal, was transfused through the normal liver, the mixture retained its ability to produce an anaphylactic reaction; but when the same mixture was passed through the liver of a sensitized animal, its power to cause anaphylaxis was lost.

In view of these facts, it seemed desirable to determine whether the relative lack of toxicity of bile in obstructive jaundice might be due to the detoxifying activity of the liver. The method previously used in studying anaphylaxis, by injecting the material to be tested first into a systemic vein and later into a branch of the portal system under controlled conditions, offered a means of determining the effect of the liver on bile.

METHOD

Ox bile was obtained from ten to fifteen gallbladders of freshly killed animals. It seemed desirable to collect the bile from a number of animals so that there

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11. Dixon, W. E., and Lee, W. E.: Tolerance to Nicotine, Quart. J. Exper. Physiol. **5**:373, 1912.

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13. Weiss, S., and Hatcher, R. A.: Studies on Strychnin, J. Pharmacol. & Exper. Therap. **19**:419, 1922.

14. Falls, F. H.: Allergic Phenomena Following Intraportal Injections, J. Infect. Dis. **22**:83, 1918.

15. Manwaring, W. H., and Crowe, H. E.: Rôle of Hepatic Tissues in the Acute Anaphylactic Reaction, J. Immunol. **2**:517, 1917.

would be more or less uniformity from day to day. The material was diluted with an equal volume of physiologic sodium chloride and injected within three hours after its collection. Each specimen of bile was used for two experiments; in one the injection was made into a systemic vein, while in the other a branch of the portal vein was used.

Dogs were used in all experiments, and an effort was made to obtain two animals of approximately the same weight to test a single specimen of bile. The dogs were anesthetized by the open drop method, and later a cannula was placed in the trachea and connected with an ether bottle. The peritoneal cavity was then opened and a needle connected with rubber tubing to a buret was inserted and tied either into a branch of the mesenteric vein or into the iliac vein, depending on the experiment. This insured an equal amount of intra-abdominal manipulation in each type of experiment. A cannula was placed in the carotid artery and connected with a mercury manometer for a blood pressure tracing. A tube was placed in the etherization system and connected with a tambour and writing lever for a tracing of the respiratory movements. The femoral artery was then exposed for the taking of specimens of blood. Bile diluted with an equal volume of physiologic sodium chloride was injected from the buret at a uniform rate of from 2.5 to 3 cc. per minute. Blood pressure and respiration tracings were made after the injection of every 25 cc. of diluted bile. Specimens of blood were taken previous to the beginning of the injection, after each 50 cc. injected, and finally at the end of the experiment. Quantitative van den Bergh [16] and calcium [17] determinations were made on the blood. In some experiments the vagi were divided to determine the effect on the cardiac arrhythmia.

RESULTS

Ten specimens of bile were tested in animals in whom the vagi were intact. Figure 1 shows the characteristic gradual fall of blood pressure which occurs when bile is injected into a systemic vein. This fall in blood pressure is later accompanied by a striking arrhythmia, and at times there is an apparent cessation of cardiac activity. Figure 2 shows the characteristic blood pressure curve when bile is injected into a branch of the portal vein. The fall in blood pressure and arrhythmia are identical with that seen in figure 1. In both curves the alterations in respiration are quite similar.

The results are summarized in table 1. The lethal dose when given into a systemic vein varied from 6.5 to 12.3 cc. per pound of body weight, while when given into the portal vein the lethal dose varied from 6.4 to 13.9 cc. per pound. The average lethal dose in the systemic vein was 8.8 cc., while in a branch of the portal vein it was 10.04 cc. per pound of body weight. This is approximately 13 per cent more in the portal than in the systemic circulation. In all the experiments tabulated, with

16. McNee, J. W.: Jaundice, a Review of Recent Work, Quart. J. Med. **16**:390, 1923.

17. Clark, E. P., and Collip, J. B.: Tisdall Method for Determination of Blood Serum Calcium with a Suggested Modification, J. Biol. Chem. **63**:461 (March) 1925.

Fig. 1.—Effect of injection of bile into a systemic vein on the blood pressure and respiration. The vagi are intact.

Fig. 2.—Effect of injection of bile into a branch of the portal vein on the blood pressure and respiration. The vagi are intact.

TABLE 1.—*Vagi Intact*

Bile Specimen	Systemic Vein: Weight of Dog, Pounds	Amount Injected, Cc.	Serum Calcium at Beginning per 100 Cc., Mg.	Serum Calcium at End 100 Cc., Mg.	Van den Bergh at Beginning	Van den Bergh at End	Lethal Dose per Pound, Cc.	Portal Vein: Weight of Dog, Pounds	Amount Injected, Cc.	Serum Calcium at Beginning per 100 Cc., Mg.	Serum Calcium at End per 100 Cc., Mg.	Van den Bergh at Beginning	Van den Bergh at End	Lethal Dose per Pound, Cc.	Bile Calcium per 100 Cc., Mg.
1	10.25	108	—	12.0	—	—	10.5	14.25	182	14.4	25.4	—	—	12.7	—
2	22.0	148	8.0	18.8	—	—	6.7	22.25	243	8.0	17.0	—	—	10.4	—
3	15.0	100	11.2	12.0	—	—	6.6	16.25	200	12.4	24.0	—	—	12.1	—
4	26.5	278	7.4	8.2	—	—	10.5	17.5	177	8.8	10.3	—	—	10.1	—
5	27.5	340	14.0	16.0	0	3.8	12.3	31.5	440	10.0	19.3	0	4.0	13.9	—
6	17.25	136	8.0	10.2	0	1.6	7.8	19.0	127	8.1	13.7	0	2.6	6.6	—
7	15.5	102	13.8	14.4	0	0.0	6.5	17.0	127	10.6	11.3	0	1.0	7.4	8.8
8	19.0	188	11.0	19.2	0	4.7	9.9	20.0	220	7.0	13.6	0	4.4	11.0	—
15	19.0	128	10.0	12.4	0	1.0	6.7	12.25	70	14.1	16.2	0	1.2	6.4	10.0
16	11.5	118	14.8	13.6	0	0.8	10.2	12.25	121	13.8	14.8	0	1.0	9.8	11.3
Average			10.9	13.7	0	1.9	8.8			10.7	16.6	0	2.4	10.04	

TABLE 2.—*Vagi Divided*

Bile Specimen	Systemic Vein: Weight of Dog, Pounds	Amount Injected, Cc.	Serum Calcium at Beginning per 100 Cc., Mg.	Serum Calcium at End 100 Cc., Mg.	Van den Bergh at Beginning	Van den Bergh at End	Lethal Dose per Pound, Cc.	Portal Vein: Weight of Dog, Pounds	Amount Injected, Cc.	Serum Calcium at Beginning per 100 Cc., Mg.	Serum Calcium at End per 100 Cc., Mg.	Van den Bergh at Beginning	Van den Bergh at End	Lethal Dose per Pound, Cc.	Bile Calcium per 100 Cc., Mg.
9	11.5	58	13.6	16.8	0	1.0	5.0	29.5	237	14.6	16.4	0	1.5	8.0	10.8
10	6.75	24	13.4	12.2	0	0.7	3.5	11.0	44	12.2	13.2	0	1.6	4.0	9.8
11	23.0	132	12.3	14.2	0	0.8	5.7	20.75	90	14.4	14.6	0	0.6	4.3	9.0
12	11.0	58	11.0	11.6	0	2.0	5.2	13.25	80	13.0	14.4	0	0.0	6.0	9.6
13	14.5	84	15.4	11.6	0	1.5	5.8	18.75	138	11.6	11.2	0	0.2	7.3	10.4
14	17.0	157	15.1	11.0	0	0.0	9.2	21.5	180	12.4	11.8	0	1.5	8.3	9.6
Average			13.4	12.9	0	1.0	5.7			13.0	13.6	0	0.9	6.3	

one exception, there was an appreciable rise of the serum calcium. The rise of calcium was greater in the dogs which received bile in the portal vein. In the latter there was an increase of 55 per cent, while in the former the rise was but 25 per cent. In the twelve animals on whom van den Bergh determinations were made, there was a rise in eleven.

VAGI DIVIDED

Six specimens of bile were tested in animals after division of the vagi to determine whether the arrhythmia could be eliminated by this procedure. The results are summarized in table 2. The average lethal dose given into a systemic vein was 5.7 cc., and in the portal vein it

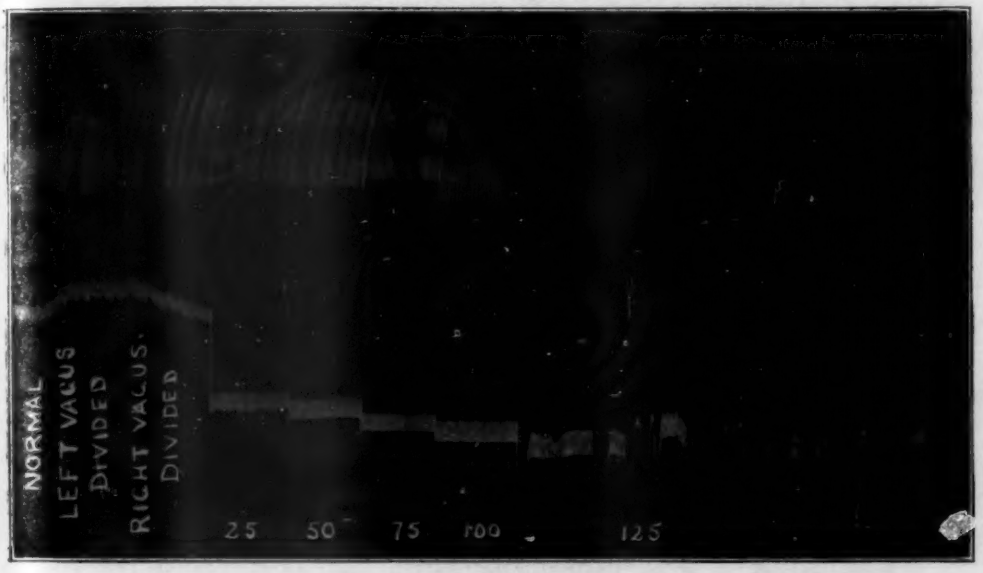

Fig. 3.—Effect of injection of bile into a systemic vein on the blood pressure and respiration. The vagi are divided.

was 6.3 cc. per pound of body weight, a difference of 10.5 per cent, which is comparable to the difference noted when the vagi were intact. The cause of this diminution of the lethal dose is not known. Additional trauma may be a factor. In these experiments the elevation of the calcium in the blood was not so striking, but this may have been due to the injection of smaller quantities of bile. Of the twelve animals, ten showed a rise in the van den Bergh determinations of the blood.

Figure 3 shows the characteristic change in the blood pressure during the injection of bile into a systemic vein when the vagi are divided. There is a similar gradual fall in blood pressure to that seen when the vagi are intact, with a gradually developing arrhythmia which continued until death. Figure 4 shows the changes which occur when the

bile is injected into the portal vein with the vagi divided. This curve is similar to that seen in figures 1, 2 and 3.

COMMENT

The fact that the lethal dose of bile given at a uniform rate is 13 per cent higher when injected into a branch of the portal vein than when given into a systemic vein does not necessarily indicate that the bile has been detoxified by the liver or that some toxic element has been removed. It is generally believed that death in such experiments is due to direct action of bile on the myocardium. In those experiments in which the bile was injected into the iliac vein, it was carried directly to

Fig. 4.—Effect of injection of bile into a branch of the portal vein on the blood pressure and respiration. The vagi are divided.

the right side of the heart in great concentration, and accordingly the action was more direct. Bile injected into a branch of the portal vein was first carried to the liver, where more even dilution occurred in the capillary bed, and on its return to the right side of the heart through the hepatic vein the concentration would not be so great. This explanation seems more reasonable because of the relatively slight difference in the toxicity of bile injected by the two routes.

The rise of the serum calcium at the conclusion of the experiments was a uniform result. The significance of this is not known. The average calcium content of nine specimens of mixed bile was 9.9 mg. per hundred cubic centimeters. Accordingly, the elevated blood calcium could not be attributed to the calcium content of the injected material.

It is interesting to note that the cardiac arrhythmia developed, whether the vagi were intact or divided. Since the effect of atropine was not tested, the conclusion cannot be drawn that the arrhythmia was entirely of myogenic origin from direct action of the bile.

CONCLUSIONS

1. The liver shows little, if any, tendency to detoxify bile when injected into a branch of the portal vein.

2. There is a fairly uniform and rapid rise of serum calcium following the intravenous administration of bile.

3. Death may occur following the intravenous injection of bile before the van den Bergh reaction is appreciably elevated.

4. Division of the vagi does not eliminate the arrhythmia of the heart.

RELATION OF THE PYLORUS TO DURATION OF EXPERIMENTAL GASTRIC ULCER *

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Efforts to produce chronic gastric or duodenal ulcers experimentally have met with indifferent success so far as any direct bearing on ulcers in the human stomach is concerned. Dogs, the experimental animals usually employed for this purpose, are notoriously immune to ulcerations of this nature, unless complex procedures are employed by which the normal physiology is so disturbed that conclusions cannot be drawn with any great accuracy. In recent years chronic experimental ulcers have been produced, notably by Dragstedt and Vaughn,[1] Hanrahan in an experimental study as yet unpublished, Mann [2] and his co-workers and Wolfer.[3] Any bearing that these reported experimental results may have on the subject would seem to be applicable more to the postoperative ulcer than to the primary one. Wolfer's experiments in which he produced ulcerations by exposing gastric mucosa over long periods of time to the roentgen ray, though of interest, apparently do not have any bearing on the general problem of ulcers. The production of experimental ulcer with streptococci, the selective theory of Rosenow,[4] the use of isogastrotoxin and iso-enterotoxin in the production of ulcers by Myagawa [5] et al. and Nakashima's [6] interesting corroboration of the "spasmogenic theory" need not be considered at this time.

In the course of experiments instituted to throw possible light on the etiology of primary ulcerations of the stomach and duodenum, incidental facts developed which seemed worthy of reporting. In 1916

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* From the Surgical Hunterian Laboratory of the Johns Hopkins University Medical Department.

1. Dragstedt, L. R., and Vaughn, A. M.: Gastric Ulcer Studies, Arch. Surg. **8**:791 (May) 1924.

2. Mann, F. C., and Williamson, C. S.: Experimental Production of Peptic Ulcer, Ann. Surg. **77**:409, 1923.

3. Wolfer, J. A.: Chronic Ulcer of the Stomach, Its Experimental Production and Its Effect on Gastric Secretion and Motility, Ann. Surg. **84**:89, 1926.

4. Rosenow, E. C.: Etiology of Spontaneous Ulcer of Stomach in Domestic Animals, J. Infect. Dis. **32**:384, 1923.

5. Myagawa, Y.; Murai, H., and Terada, M.: Experimental Study of Cells of Mucous Membrane of Digestive Tract as Toxin or Irritant and Their Relation to Formation of Peptic Ulcer, Japan M. World **3**:136, 1923.

6. Nakashima, Y.: The Pathogenesis of Peptic Ulcer of the Stomach and Duodenum. Experimental Contributions on von Bergmann's Spasmogenic Theory, Ztschr. f. d. ges. exper. Med. **42**:4, 1925.

Bolton [7] found that ulcerations of the gastric mucosa produced by the intravenous injection of foreign proteins persisted for a much longer period if the pylorus was almost completely closed. About the pyloric ring he sutured rubber bands, which, though offering definite resistance to the passage of food through the pylorus, nevertheless would not effect complete occlusion. It has long been known that definite types of abdominal diseases manifest themselves to a large extent through the activity of the stomach. These manifestations, such as epigastric pain and vomiting, are due wholly to spasmodic contractions of the entire stomach and consequently of the pyloric sphincter. I [8] have shown in a previous paper that irritation of the parietal or visceral peritoneum in experimental animals will produce a pylorospasm which manifests itself by a greatly delayed emptying time of the stomach. It was suggested that the peritoneum may be regarded as the receptor mechanism of the reflex arc, and, as has further been shown, the efferent part of this reflex lies wholly within the vagus trunks.[9] Demonstration of the latter fact was made by dividing the vagus trunks at the cardia and also the gastric branches of the vagus, after which it was impossible to produce a reflex pylorospasm by peritoneal irritation. The relation of reflex spasm to the development of gastric ulcer suggests itself, in view of the fact that when many patients present themselves they have fully developed gastric or duodenal ulcers and give a long preliminary history attributable to chronic inflammation of some abdominal viscus, most commonly the appendix or gallbladder. Recent reports indicate such an association in 80 per cent of all cases. Monsarrat [10] and others have drawn attention to the significance of the factor of wear and tear on the pyloric antrum and on the first portion of the duodenum in the causation of ulcers. The prompt relief of symptoms and decrease in size of pyloric and duodenal ulcers following gastro-enterostomy is, of course, generally known. The curative effect of gastro-enterostomy is probably not due to any chemical change of the gastric juice, resulting from the operation, but rather to the effect of division of the circular muscle fibers in the antral portion of the stomach. Furthermore, a properly performed gastro-enterostomy supplies to the stomach immediate and efficient drainage, thus doing away with the factor of retention due to a spastic pylorus. A proper understanding of this retention is necessary for a full appreciation of its effect. The retention does not necessarily mean

7. Bolton, C.: Ulcer of the Stomach, London, Edward Arnold, 1916.

8. Hughson, W.: Reflex Spasm of the Pylorus and Its Relation to Diseases of the Digestive Organs, Arch. Surg. **11**:136 (July) 1925.

9. Hughson, W.: The Effect of Vagus Neurotomy on the Pyloric Sphincter, J. A. M. A. **88**:1072 (April 2) 1927.

10. Monsarrat, K. W.: The Etiology of Gastric and Duodenal Ulceration, Brit. M. J. **1**:521, 1926.

a total increase in the emptying time, but rather delay in emptying during any phase of the digestive cycle, or emptying at the expense of more vigorous muscular effort on the part of the stomach required to overcome the spastic contraction of the pyloric sphincter. The common roentgen-ray picture of a hyperactively contracting stomach is evidence of this fact, for peristaltic waves of the stomach itself cannot be increased in frequency and amplitude without a corresponding hyperactivity of the pylorus. Sphincter musculature can manifest hyperactivity in only one way—that is, by spasm.

The experiments detailed in the protocols were undertaken, therefore, to demonstrate what relation such pylorospasm might have on the development of ulcers in experimental animals. In previous experiments in which pylorospasm was produced, there had never been any indication of the development of ulcers, so that it was obviously impracticable to expect these ulcers to develop spontaneously. Also it seemed doubtful that an experimentally produced pylorospasm would persist long enough to make any particular differentiation possible. It appeared feasible, therefore, to occlude the pyloric opening partially, by almost any method, and to study its effect on an ulcer made experimentally, controlling the observation on animals whose pylorus was intact. The familiar and easy method of injecting silver nitrate into the submucosa was chosen for the production of the ulcers. This proved not entirely satisfactory, so that later a small section of gastric mucosa was excised, about 1 cm. in diameter, and the submucosa infiltrated with silver nitrate directly. At first an opening was made on the anterior wall of the stomach about 8 to 10 cm. proximal to the pylorus, and the procedure I have described was carried out at a point about 2 cm. proximal to the pylorus on the anterior wall. These ulcers all healed so rapidly that definite conclusions could not be drawn. Later the ulcer was made on the lesser curvature at a point about 2 cm. proximal to the pylorus, and a striking difference was noted, as the ulcer developed a fair comparative degree of chronicity. The method of partially occluding the pylorus consisted of a procedure which might be termed a reverse Rammsteadt operation. In other words, an incision was made on the anterior wall of the pylorus parallel to the circular fibers, the submucosa drawn out and a continuous silk stitch applied through a section of this layer for about 1 cm. parallel to the long axis of the stomach, and the incision through the muscle was closed in the opposite direction as in the Mikulicz operation. Animals were operated on in pairs, the pylorus being occluded in one and not in the other, while each had an ulcer or defect in the mucous membrane produced on the lesser curvature. These ulcers were either entirely removed at subsequent operation, or else the animals were killed and the ulcers examined.

Contrary to expectation, in the first group of animals the ulcers in those whose pylorus had supposedly been decreased in size were found

almost completely healed when the sections were removed. Up to this time no fluoroscopic control of the stomach had been made. Following this observation, animals subsequently operated on were examined fluoroscopically on several occasions, following operation, and a rather unexpected fact was demonstrated. The emptying time of the animals whose pyloric ring had been divided and sutured was much shorter than those whose pylorus was intact, shorter in fact than the normal of three and four-tenths hours. After some consideration, the explanation appeared fairly obvious. In those animals in which a partial occlusion of the pylorus had been attempted the continuity of the sphincter had been destroyed, and the suture of the submucosa had resulted actually in splinting the opening rather than occluding it.

Although the immediate effect may have been to delay emptying, this was promptly overcome, and the result amounted to a permanent opening rather than one which went into phases of contraction and relaxation, a condition analogous to the rapid emptying found in annular tumors of the pyloric end of the stomach before the obstruction stage. Furthermore, in those animals whose pylorus had been left intact, a definite delay in the total emptying time of the stomach was noted. The explanation here was immediately clear, as the production of the experimental ulcer and the opening made in the anterior wall of the stomach produced peritoneal irritation and consequent hyperactivity or pylorospasm. Wolfer made a similar observation in his animals with roentgen-ray ulcers, but attributes the effect—wrongly, I believe—to "involvement of the local intrinsic mechanism by the ulcer placed close to the pylorus." On the basis of these observations, a series of sixteen animals was used, half of which had what must now be spoken of as pyloric fixation and the other half an intact pylorus. These animals in pairs were killed at varying intervals of time after fluoroscopic controls had been made to confirm further the observations mentioned. This confirmation was obtained in every instance. The longest period of time elapsing between original operation and killing the animal was seven weeks. The remaining animals were killed at varying periods, the shortest being three weeks. Typical protocols of such experiments follow:

PROTOCOL 1.—Dec. 2, 1925: Dog, brown, female. Anesthetic, ether. Operation, decreasing size of pylorus.

High right rectus incision. Pylorus exposed. Incision through musculature parallel to sphincter, exposing submucosa. Fine silk running suture through submucosa for distance of about 5 mm. This incision closed in opposite direction, thus decreasing diameter of pylorus. Good condition. Closure with silk.

Jan. 26, 1926: Animal rather thin.

2:30 p. m.: 300 cc. barium solution by stomach tube.

2:40: Fluoroscopic examination. Waves active, but pylorus shows definite constriction. Just proximal to pylorus is pouch about 1 cm. in diameter, which

is distended as waves advance toward pylorus. Small amount of barium in intestine.

4:25: Almost empty.

March 8, 1926: Operation, laparotomy. Excision of small area of mucous membrane on anterior surface proximal to pylorus. Injection of 1 cc. 10 per cent silver nitrate solution.

April 1, 1926: Operation, laparotomy. Stomach opened, but impossible to find even a scar indicating point at which mucous membrane was removed. One area which seemed rather pale was removed for section.

In this experiment with an emptying time of two hours in an animal whose pylorus had been splinted, practically complete healing of the ulcer took place in the brief period of three weeks.

PROTOCOL 2.—April 7, 1926: Dog, brown, male. Anesthetic, ether.

High right rectus incision. Anterior wall of stomach opened 6 cm. from pylorus. Area of mucous membrane 1 cm. in diameter removed on lesser curvature. Injection of 1 cc. 10 per cent silver nitrate into submucosa. Stomach and abdomen closed.

April 14, 1926: 2:30 p. m.: Fluoroscopic examination. Three hundred centimeters barium solution by stomach tube.

4:30 p. m.: Still half full. Marked delay in emptying. Smaller crater can be seen on lesser curvature.

Stomach examined through high right rectus incision. Ulcer 1 cm. in diameter on lesser curvature. Examined through opening on posterior wall of stomach. Wound closed.

May 3, 1926: Animal dead of distemper. Autopsy. Marked ulceration on lesser curvature. Some crater formation with slough. Little evidence of healing.

This ulcer is shown in figure 5. With no splinting of the pylorus a delay in the emptying time was observed, and the experimental ulcer showed little indication of healing at the end of approximately four weeks.

The results were remarkably uniform in their general outcome. Microscopic sections of the ulcers were examined in the majority of cases, but added nothing particular to the information obtained from the gross appearance. The ulcers cannot in any sense be compared to the chronic ulcer in the human stomach, but simply represent a defect in the mucous membrane with a slough developing in the submucosa, with some crater formation and a chronic inflammatory reaction in the immediate surrounding tissues. Healing takes place by a separation of the slough in the submucosa, cicatrization of the defect thus made and covering over of the area with mucous membrane.

Figure 1 represents an ulcer approximately 1 month old in an animal whose pylorus had been splinted and which had a normal emptying time. It can be seen that this ulcer is practically healed, although there is marked scarring and thickening of the wall of the stomach evident in the lateral view. Figure 2 represents one of the earlier experiments in which the ulceration was made on the anterior wall of the stomach.

Fig. 1.—Ulcer produced by injection of silver nitrate through the wall of the stomach; duration, one month. Pylorus splinted. Upper view shows scarring in the mucous membrane, lower view thickening of the submucosa.

Fig. 2.—Ulcer on anterior wall of the stomach next to the suture line. Ulcer practically healed in three weeks. Pylorus splinted.

Fig. 3.—Ulcer on the lesser curvature in animal with intact pylorus; three weeks' duration.

This ulcer had practically healed in three weeks. The pylorus was also fixed in this animal. Figure 3 is the ulcer resulting from the experimental procedure carried out on the lesser curvature in an animal whose pylorus had remained intact. Three weeks had elapsed between the operation and killing the dog. It will be noted that the defect in the mucous membrane is here of considerable size, although the slough in the submucosa is not so apparent. The control in this experiment died of distemper one week following the original operation. Figures 4 and 5 represent experiment and control, figure 4 showing the appearance of the ulcer in an animal whose pylorus had been fixed. The defect in the mucous membrane is still evident, but the slough in the submucosa has healed over almost entirely. The relation of the ulcer in figure 5 to the pyloric sphincter is evident, the duodenal mucous membrane showing clearly to the left of the picture. Here a large slough, about 1 cm. in diameter, is still apparent, this tissue being necrotic and showing marked inflammatory reaction. There has been no attempt on the part of the mucous membrane to cover the defect. Figure 6 shows the experiment and control again. The control observation is shown at the top with the ulceration practically healed and the mucous membrane markedly puckered. The effect of splinting the pylorus is seen at the left. In the lower figure the ulcer is still active, in the middle there is a definite slough, and the mucous membrane has made but little progress in the process of covering the defect. These animals both remained alive and well for seven weeks following the original operation.

COMMENT

From the data obtained in these experiments and the description of the drawings, certain facts seem fairly evident. Experimentally produced defects in the gastric mucous membrane with an injection of 10 per cent silver nitrate into the underlying submucosa require a longer time to heal, if the pylorus is intact, than those produced in a stomach with a splinted pylorus. In the foregoing discussion these defects have been referred to as ulcerations. The propriety of such an appellation is, of course, dubious, but doubtless it is as nearly correct as the term used in connection with the intravenous injection of streptococci or in Dragstedt and Vaughn's experiments in which mucous membrane was excised and silk stitches were left hanging from the submucosa. Too free interpretation of experimental results in terms of human pathology is a pitfall which should be carefully avoided. The very difficulty experienced by all investigators in producing experimental ulcers in dogs is evidence enough of this danger.

The reflex mechanism of the pyloric sphincter in dogs does, however, behave in a manner similar to that seen daily in clinical medicine and surgery. As has been stated, hyperactive muscular contraction of

Fig. 4.—Ulcer in animal with fixed pylorus. Slough had separated, and defect had almost healed in submucosa; one month's duration.

Fig. 5.—Companion to figure 4. Animal with intact pylorus. Extensive slough in submucosa; one month's duration. Pyloric ring and duodenal mucous membrane seen to left of illustration.

Fig. 6.—Experiment and control, seven weeks' duration. Upper view of specimen from animal with fixed pylorus. This can be seen to the left of the picture. Ulcer on lesser curvature practically healed. Lower view of the intact pylorus with ulcer still present. Crater-like defect in submucosa.

the stomach is undoubtedly responsible for a large number of the symptoms of all abdominal diseases. This hyperactivity must manifest itself by pyloric contraction, and a delay in emptying of the stomach, either total or relative, results. The establishment of proper drainage of the stomach in the presence of ulceration, whether benign or malignant, results always, no matter what the method employed, in a prompt subsidence of the organic reaction and in many instances in actual cure of the ulceration. This being true, it is entirely reasonable to suppose that the opposite condition, delayed emptying or poor drainage, should be largely responsible at least for the growth of the ulcer. Reference to its part in the actual etiology is purposely avoided at this time. The experimental observations outlined herewith amply confirm this opinion, for evidence has been brought forward to show that experimental ulcers with an intact pylorus cause delay in emptying. When the emptying is hastened, and this was not as the expense of greater muscular effort but simply by splinting the pyloric sphincter, the ulcers healed in a minimum length of time. Chemical studies have not been made, for if there were changes in the gastric juice, this also would be caused by the delayed emptying. The extremely high acid values found in complete pyloric obstruction is the most striking example of this particular cause and effect.

It is believed, therefore, that the relationship between duration and possibly severity of ulceration of the stomach and the emptying of the stomach has been demonstrated experimentally. Furthermore, presumptive evidence is advanced to indicate that this factor of emptying plays an extremely important rôle in the whole life history of the ulcer. Though possibly nothing in the way of actually new information is brought forth by this demonstration, nevertheless one of the many vaguely appreciated clinical concepts has been given adequate experimental support.

CONCLUSIONS

1. Experimentally produced ulcers on the lesser curvature of the dog's stomach result in a delayed emptying of the stomach in the presence of an intact pylorus.

2. Splinting of the pylorus in these experimental animals obviates this delayed emptying.

3. In the animals in which delay is demonstrated, ulcerations remain active at least twice as long as in the group in which the emptying is more rapid.

4. This delay is due to reflex contraction of the pyloric sphincter.

COALITION OF THE CALCANEUS AND THE NAVICULAR

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Rigid flatfoot is generally considered to be the result of prolonged eversion and abduction, unrelieved by treatment. A failure of proper balance of the foot because of congenital or acquired weakness is considered the primary fault. The mechanism of the development of the alteration in relationship to the tarsal bones is dependent on the faulty position of the foot, which throws excessive and prolonged strain on ligamentous structures. The ligaments are not physiologically capable of resisting prolonged strain, and give way, allowing the tarsal bones to rotate into the typical deformity of flatfoot. The altered position of the tarsal bones and their articulations tends to produce a rigid foot.

Although the rigid foot is less mobile than the normal one, it is frequently asymptomatic. In some cases, however, the foot remains painful, and the rigidity is greatly exaggerated by muscle spasm, chiefly of the peroneal group. This condition produces more or less severe disability, which can frequently be relieved by appropriate treatment by standard methods.

At the University Hospital there have been a few obstinate cases in which cure has not resulted. The treatment was based on the accepted doctrine that the mechanism of the development of the rigid flatfoot with peroneal spasm was dependent on a primary defect in the soft tissue with a secondary alteration in the skeleton of the foot. This assumption proved fallacious, for there is another mechanism for the development of the rigid flatfoot, which is not generally considered. A review of the resistant cases, in which the patient did not improve under the standard therapy, demonstrated a malformation or deformity of the calcaneus or navicular, which in this group undoubtedly is the primary cause for the development of a rigid foot. In these cases, the rigid foot was not produced by a primary failure of the soft tissue with a secondary change in bone, but rather by a primary abnormality in the growth of the bone with secondary change in the soft tissue.

My first conception of the possibility that rigid flatfoot results from a congenital abnormal formation of the bone was obtained from an article by Slomann,[1] of Copenhagen. Slomann was apparently the first to recognize the condition clinically. He reported five cases in an article entitled "On Coalitio Calcaneo-Navicularis," which appeared in 1921.

1. Slomann: On Coalitio Calcaneo-Navicularis, J. Orthop. Surg. **3**:586, 1921.

In his article, he gives Holl, of Vienna, credit for first observing the coalition in two cases examined in the anatomic laboratory.

The knowledge of the etiology of the bony fusion between the calcaneus and navicular is derived from a study by W. Pfitzner, of Strassburg. Pfitzner believed the coalition must arise from abnormal

Fig. 1 (case 2).—Coalition of the calcaneus and navicular complete. An excellent illustration of complete fusion with a bony bridge.

Fig. 2 (case 2).—The normal foot of the same patient, showing no roentgenologic evidence of a calcaneus secundarius.

development of the tarsalia. He studied skeletons of 840 feet, and found the development of a tarsal bone, the calcaneus secundarius, in nine, or 1 per cent of the cases. Slomann quotes Pfitzner freely in describing the development of the calcaneus secundarius into the various stages of coalition.

At that point of the tarsus skeleton where the processus anterior calcaneus, the cuboideum, the navicular and the caput tali meet, without, however, all coming into direct touch, is to be found, with careful dissection, in a certain number of cases, a little bone of irregular shape, the so-called calcaneus secundarius. This tarsale appears symmetrically in that when present it always appears in both feet. Its size and independence may differ greatly in the two feet. In the more developed tarsale four surfaces facing the four bones mentioned can be made out. The surfaces facing the talus and cuboideum are

Fig. 3 (case 4).—The fusion of the calcaneus secundarius to the calcaneus in the right foot is shown here. The development is not large, but it produced definite symptoms. The bilateral appearance of the tarsale is shown in this case and also the tendency toward an asymmetrical development.

Fig. 4 (case 6).—Fusion of the calcaneus secundarius to the navicular, with almost complete coalition of the calcaneus to the navicular. The coalition is probably complete, with the clear area between the two processes a cartilaginous band.

articular surfaces, while those facing the processus anterior calcanei and the navicular are attached to these bones by a fibrous tissue. If the calcaneus secundarius is strongly developed, it in this way forms a bridge between the calcaneus and navicular, and if now it follows the tendency of the inconstant tarsalia to fuse to the neighboring bones, it may show itself either, as is most usual, as a protuberance on the calcaneus (fig. 3) or as a protuberance on the navicular (fig. 4), or finally, *if it attaches itself closely to both, as a coalitio-calcaneo navicularii* (figs. 5, 6, 7 and 8).

"Pfitzner has described 15 cases himself of such coalition, and has collected 38 from the literature." Holl and Slomann emphasized the presence of the abnormality associated with flatfoot. Pfitzner denies the necessary association of the coalition with flatfoot. In the group of cases in the University Hospital rigid flatfoot with peroneal spasm

Figure 5

Figure 6

Figs. 5 and 6 (case 1).—Fusion of the calcaneus secundarius to the anterior medial end of the calcaneus with practically complete coalition to the navicular. The clear space is not an articulation, but cartilaginous tissue.

was constantly present. Slomann believes "the deformity to be due to the manner in which the anterior component of the body weight, acting downward and forward through the corpus tali, is transmitted through the caput tali to the navicular and then stopped up by the coalition, is

transferred directly to the foremost and innermost point of the calcaneus (instead of, as in normal conditions, being transmitted from the navicular forward through the cuneiforme I to the metatarsale I), which rotates the calcaneus inward and lays its foremost part down flat against the ground." It is also quite possible that either the complete osseous union, or the union of the calcaneus secundarius to the navicular or calcaneus may alter the relation of the tarsus during the growth of the skeleton of the foot. The latter theory is supported some-

Fig. 7 (case 5).—Roentgenogram made from the oblique position shows the solid bony bridge connecting the calcaneus and navicular, a true coalition.

Fig. 8 (case 5).—Roentgenogram made in the anterior-posterior position shows the definite coalition of the calcaneus and navicular.

what by the marked uniformity of appearance of symptoms at the age of puberty.

During the past year, I have seen five cases which showed various stages in the fusion of the calcaneus secundarius, from the stage of fusion to the anterior medial end of the calcaneus, to the formation of a complete bony bridge between the calcaneus and navicular. In all of these cases there was a severe disability of the affected foot with pain and discomfort when it was used. The rigidity of the foot was in

proportion to the amount of fusion, but in all cases lateral mobility was definitely limited. Motion of the ankle joint proper was unaffected in all cases. Peroneal spasm was present in all cases.

In only one case did the patient respond favorably to the standard methods of treatment used for pronated rigid foot with peroneal spasm. It is not known whether this patient obtained complete relief, as he

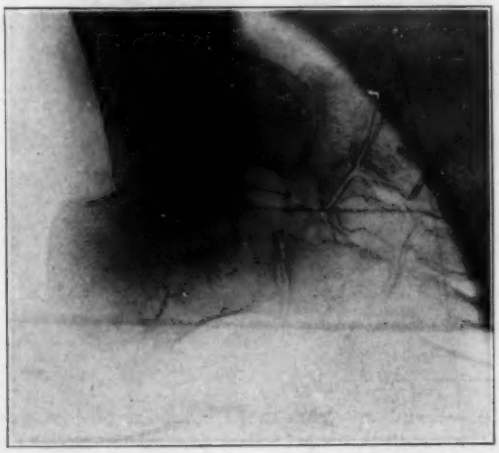

Fig. 9 (case 5).—Postoperative roentgenogram made from oblique position showing resection of bony bridge. The markedly increased separation of the cuboid from the navicular is now obvious, as is also the relation of the external cuneiform to the bony bridge.

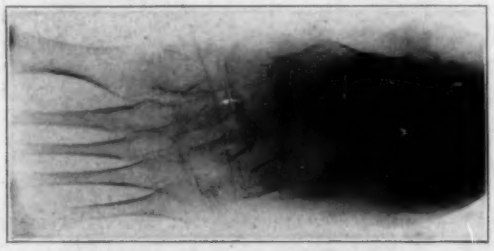

Fig. 10 (case 5).—Postoperative roentgenogram from anterior-posterior position demonstrates removal of bony bridge and illustrates its relation to the tarsal bones.

returned to the clinic but once after the treatment was instituted. The other four patients showed no improvement. In two cases lengthening of the peroneal tendons in addition to repeated manipulations to correct the deformity, followed by retention in bivalved plaster casts, and by the usual postoperative massage, exercises and other forms of physiotherapy, failed to give relief. Two patients who showed a definite

bony bridge between the calcaneus and the navicular were treated by operation planned to eradicate the primary deformity of the bone. It is too early in either of these cases to state the result of this form of therapy, but present evidence points toward satisfactory results in both. The procedures employed with the results, are discussed in the abstract of the case (figs. 9, 10 and 11).

I have an additional case of partial coalition of the calcaneus and the navicular, which was seen in the clinic some years ago. A lantern

Fig. 11 (case 2)—Foot of patient in case 2 following resection of bony bridge and arthrodesis of the subastragaloid and astragaloscaphoid joints.

Fig. 12 (case 5)—Roentgenogram made from the lateral position gives little idea of the coalition. The malformation of the anteriomedial end of the calcaneus is obvious. Note the bony overgrowth on the talus, seen commonly in this condition.

slide of the roentgenogram was preserved by Van Zwalenberg as an interesting and rare case. I do not have the history of the patient, but the lantern slide shows the typical deformity.

The abnormal development of bone caused by the tarsal calcaneus secundarius is sufficiently frequent to warrant more general recognition. My own failure to recognize the deformity in spite of a search for it since 1920, I believe to be due to improper projection of the roentgen

ray. The usual lateral and anterioposterior roentgenogram shows the deformity poorly, as is illustrated in case 5 (fig. 12). An oblique position, as demonstrated in the illustrations, shows the abnormality well. With this roentgen-ray technic, the coalition will be observed frequently in a large clinic.

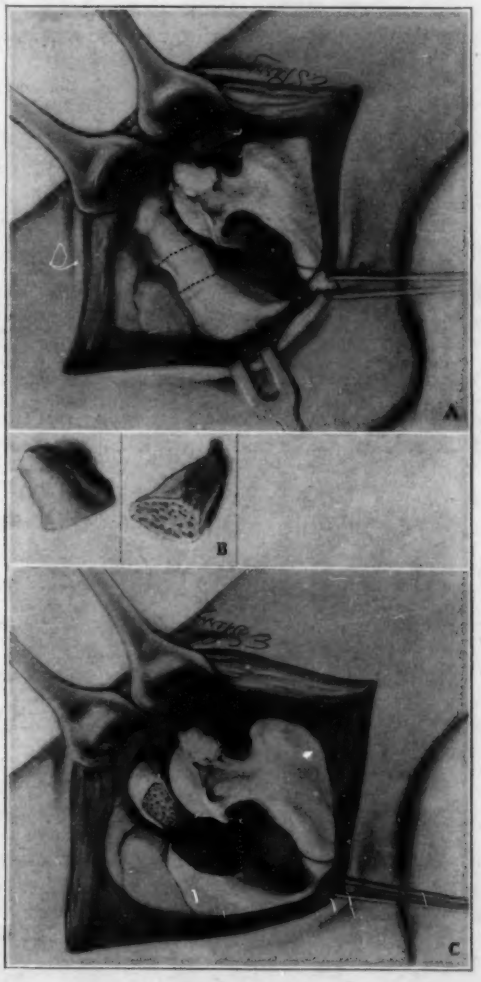

Fig. 13 (case 5).—*A* indicates the bony bridge attached to the calcaneus and navicular. The relation of the bridge of bone to the cuboid, external cuneiform and the caput tali is well shown. The bony overgrowth on the caput tali is seen on the dorsolateral surface just back of the articulation. The posterior calcaneoastragaloid joint is seen just above Allis clamp. The dotted line represents the segment of bone removed. *B* indicates the resected bony bridge; *C*, drawing made after removal of bridge.

I do not believe that the usual procedures employed for rigid flatfoot of the primary soft tissue type will be of benefit in the majority of these cases.

I do not insist on my own operative methods in the treatment of these patients, since my experience and material are too meager, and I have seen no reference to operation previously in this type of case. I feel, however, that operation in the conditions that resist conservative treatment is indicated. I believe that in the complete fusion type it is possible that a mobile foot, functionally satisfactory, can be obtained by resection of the coalition (fig. 13), if the operation is undertaken early after the onset of symptoms. If considerable delay has occurred, it is probable that traumatic changes in the subastragaloid and calcaneonavicular joints have developed which will require arthrodesis of the affected foot for relief of the symptoms.

CONCLUSIONS

1. Coalition of the calcaneus and the navicular, partial or complete, is a possible cause of rigid flatfoot, which should be differentiated from the usual type.

2. The usual routine roentgenogram does not sufficiently demonstrate the deformity. The direction of the ray should be oblique to the foot. The abnormal formation of the bone is then clearly shown.

3. There is frequently bony overgrowth on the caput tali associated with coalition that may lead to an erroneous diagnosis of arthritis as the cause of the disability.

4. The appearance of symptoms at the age of puberty is a striking factor in the clinically reported cases.

5. The failure of the customary forms of treatment for rigid flatfoot with peroneal spasm in this type of case suggests the need of more radical therapy. Lengthening of the peroneal group has proved to be of no value in my cases. Resection of the bony bridge may give a mobile functional foot. Arthrodesis of the subastragaloid calcaneonavicular and calcaneocuboid joints may be necessary in further advanced cases.

REPORT OF CASES

CASE 1.—R. V., a boy, aged 13, entered the hospital in September, 1926, with pain and deformity of the right foot. The pain had not been marked, and was present only after prolonged use. The deformity was marked, and was the reason the parents brought the child to the clinic.

Examination showed that the right leg was three-fourths of an inch (1.8 cm.) short; there was three-fourths of an inch atrophy of the right thigh and one-half inch (1.27 cm.) atrophy of the calf. There was also a splay right foot, showing marked pronation with definite peroneal spasm.

Thomas heels, an anterior wedge to the sole of the shoe and exercises were prescribed.

This patient showed a definite coalition of the calcaneonavicular joint, and operation was discussed with the father, if the conservative form of therapy proved unsuccessful.

The patient returned to the clinic on November 5, and showed some improvement. He has not been seen since.

Case 2.—E. O., age 13, entered the hospital on March 30, 1925, with a stiff, painful ankle and foot. The onset was gradual, the summer before, with no previous history of injury. There was pain if the foot was overworked, marked limitation to lateral motion and pain on walking on rough ground, but no limp or pain after walking a short time.

Examination showed a marked limitation of the subastragaloid joint, limited mediotarsal joint, free motion of the ankle joint, marked pronation with valgus deformity and peroneal spasm.

An attempt at conservative therapy was employed, with no relief.

On Aug. 27, 1926, an operation was performed through an anteriolateral incision. A well defined bridge projected from the anteromedial portion of the neck of the os calcis and had fused as one piece with the under surface of the scaphoid. The anterior and posterior facets of the astragalus were surrounded by and included in a wall of firm fibrous tissue. There was a medial rotation of the os calcis on its long axis. The bony bridge was resected. Osteochondral exsection of the articular surface of the astragalus and scaphoid and the astragalocalcaneal joints was performed. The patient's foot was placed in a plaster cast in a corrected position, and the wound healed primarily.

The patient returned to the clinic on Dec. 10, 1926. Two months after the operation there was a recurrence of the pronation deformity of the foot and a marked peroneal spasm. Manipulation under anesthesia corrected the deformity. The foot now shows good position with slight valgus. The arthrodesis is apparently solid. The patient was fitted with an inside upright, an outside T-strap and a night mold, and was told to return in three months.

This patient had a marked bony coalition of the calcaneus and navicular with a development of a periarthritis about the subastragaloid articulations. It was deemed necessary to perform the arthrodesis because of changes in the joint.

Case 3.—E. S., a Finnish girl, aged 17, entered the hospital on July 14, 1925, complaining of pain in the right foot, with difficulty in walking. The onset had occurred five years before, following a twisting of her ankle. She had had mild symptoms since this injury, which had increased recently. There was dull pain, only occasionally sharp, worse in the morning and in hot weather (fig. 14).

Clinical examination showed a spastic, rigid flatfoot in marked pronation; active and passive attempts at inversion were impossible. There were tenderness over the scaphoid and marked peroneal spasm. The condition was considered a rigid flatfoot with peroneal spasm secondary to arthritic changes in the tarsal bones.

On Sept. 8, 1925, the patient had an operation to lengthen the peroneal tendons, followed by wrenching of the foot under ethylene anesthesia, and the application of a plaster cast to maintain varus cavus correction. The cast was bivalved. Baking and exercises were instituted after healing of the operative wound. A correction of the deformity was not obtained by this procedure, so on October 14 another manipulation was attempted. The patient was apparently somewhat relieved by this treatment, and was discharged wearing Thomas heels and stiff shank shoes, to continue her exercises.

She returned on Aug. 13, 1926, with a recurrence of the deformity and symptoms. Manipulation under anesthesia was again performed. Audible breaking up of adhesions and apparently a good correction of the deformity was obtained.

The patient has not been seen in the clinic since this manipulation.

The roentgenograms of this patient's foot show a very definite calcaneus secundarius with a fusion to the anterior medial end of the calcaneus. I believe a subastragaloid arthrodesis will be necessary in this case.

Fig. 14 (case 3).—Partial coalition. Fusion of the calcaneus secundarius to the anterior medial end of the calcaneus. The long projection and malformation of this portion of the calcaneus is clearly shown. The spur formation on the caput tali is frequently seen in these cases. There is no contact with the navicular.

Fig. 15 (case 4)—The process in this case is much more developed and the flatfoot more marked. Note the tendency for spur formation on the caput tali and the navicular.

Case 4.—R. M., a girl, aged 15, entered the hospital on Oct. 28, 1925, complaining of painful feet. The patient was well developed and obese and walked with a definite limp. She said that she had always had trouble with her feet and was unable to walk any distance without pain. Standing for any period of time was painful.

Examination showed a marked pes planus deformity with definite peroneal spasm.

The peroneal tendons were lengthened in both feet in September, 1925. Plaster casts were bivalved so that physiotherapeutic measures could be employed. Casts were removed on November 29, and Thomas heels and exercises were prescribed.

The patient returned on May 17, 1926, with some relief from pain, but still having symptoms. On June 11, 1926, both feet were manipulated under anesthesia with an unsatisfactory correction, and on July 17, 1926, a second manipulation was performed.

This patient has a definite fusion of the calcaneus secundarius to the anterior medial surface of the calcaneus. An arthrodesis of the subastragaloid joint will doubtless be necessary before she obtains relief from symptoms (fig. 15).

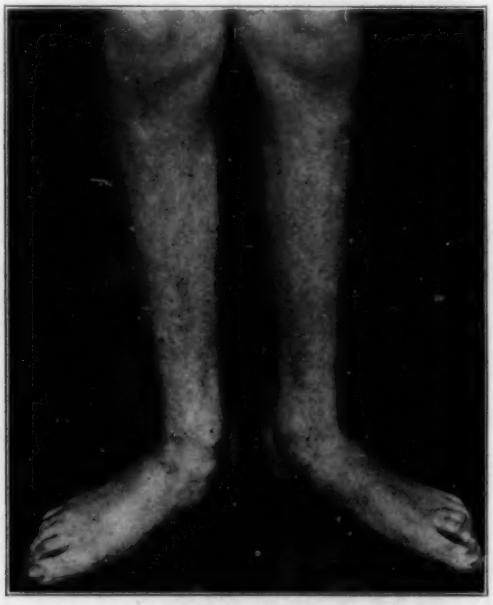

Fig. 16 (case 5).—Photograph made before operation. The pronation of the feet, more marked in the left, is obvious.

Case 5.—A. McK., an American girl, age 13, entered the hospital on Aug. 12, 1925, with pain and swelling of the right knee (figs. 16 and 17). She gave a history of pain in the left ankle a year before. This gradually disappeared, and the right knee later became involved. There was a definite synovitis of the knee with increased fluid and slightly thickened synovial tissue, but with little loss of motion.

Two months after entering the hospital the patient complained of pain in the left ankle and difficulty in walking. The left foot was held in marked pronation. Active and passive supination was impossible because of marked rigidity and peroneal spasm. There was a definite atrophy of the calf muscles.

On Nov. 12, 1926, an attempt was made to correct the deformity by manipulation under anesthesia. Inversion could not be obtained, but a cast was applied and bivalved so that physiotherapy could be instituted.

Fig. 17 (case 5).—Postoperative photograph of left foot, demonstrates increased varus and correction of pronation.

Fig. 18 (case 5).—Postoperative photograph demonstrates approach employed and the absence of peroneal spasm. Active inversion is possible.

Two months later there was no evidence of any improvement in the condition, and a roentgenogram demonstrated evidence of the bony bridge between the anterior processes of the calcaneus and the navicular.

An operation was performed on Jan. 17, 1927. An anteriolateral incision was used, exposing a bony bridge attached to the anteromedial surface of the os calcis into the lateral inferior portion of the navicular. There was a curious cauliflower-like bony overgrowth at the border of the cartilage on the dorsolateral surface of the head of the talus. The external cuneiform and the cuboid articulated with the bony bridge. The interval between the anterior end of the calcaneus and the navicular was greatly increased. The subastragaloid joint was normal in appearance. The bony bridge was removed from the navicular and the calcaneus. Following its removal, the foot was perfectly mobile, and complete inversion could be obtained. In view of the normal appearance of the articulations, no attempt was made to perform arthrodesis on the subastragaloid joint. The wound was closed in layers, and a plaster cast was applied with the foot in marked inversion and supination.

The patient had an uneventful convalescence. The wound healed by primary union. The patient could hold the foot in inversion actively ten days following the operation, and could stand with the foot well corrected. The patient was discharged with a bivalved plaster to wear at night, and with an outside upright and inside T-strap attached to a shoe that had a Thomas heel and a wedge on the inner sole.

This patient had a definite bony bridge between the calcaneus and navicular, which was the cause of the rigidity of the foot. It is too early to tell whether the correction of the deformity will be permanent, but I anticipate success.

Case 6.—R. was seen in the University Hospital some years ago, and I can find no record of the history. I have only a lantern slide which was saved by Van Zwalenberg as demonstrating a rare and interesting condition.

DEPOSITION OF CALCIUM SALTS IN AREAS OF CALCIFICATION

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In former papers I have reviewed evidence as to the manner of the transport of calcium salts in the blood stream and their deposition in bone and in calcified areas. The deposition of calcium in bone is in an extremely fine form and in such a manner that from appearances alone it might be interpreted according to the bias of the observer, either as a secretory phenomenon of the osteoblasts and bone cells or as a precipitation phenomenon. Correlated with physiologic evidence, however, the balance of proof is in favor of the secretory view. The object of this investigation, was to learn whether such was also the case in areas of calcification. In this paper I shall review the information I have obtained by the examination and study of various calcified areas, and shall discuss the conclusions to be made from the facts presented.

MATERIAL

All of the material used for this investigation was human and consisted of sections of arteries varying in size from that of areas of the wall of the aorta to that of vessels such as the radial and ulnar arteries. Calcified areas of choroid plexuses of the brain, also parts of the pineal gland and the thyroid gland were investigated.

TECHNIC

In all cases the purpose was to examine undisturbed calcium deposits, and so the specimens were only rarely decalcified, and then only for examination in conjunction with similar ones in which the calcificed areas were left intact. It is possible to cut areas of calcification if they are not too heavy, and sections from 10 to 20 microns thick were obtained. Of course, the sections tend to break up and are not perfect, but even the fracturing of the calcified areas gives valuable information at times. It is well to reserve an old microtome knife for this work alone, as the edge is necessarily spoiled.

The great majority of specimens were preserved in solutions of formaldehyde or of formaldehyde-saline. Hematoxylin, eosin and also Mallory's triple stain were usually employed. Methylene blue, Schmorl's stain and others were used occasionally. By fixing precipitates of calcium carbonate and calcium phosphate to cover-glasses and subjecting them to all of the processes of embedding and staining, I have previously shown that no alteration was occasioned in these precipitates; so it may be assumed that any masses of calcium deposits seen in any sections are in the same form after the preparation of the sections as they were previous to the manipulations.

In every case, sections of a specimen were mounted clear and unstained, in addition to those stained in various ways. By this means it was possible to make a good dark-field examination of many specimens in addition to the usual light-field examination.

EXAMINATION OF CALCIFIED AREAS

Calcification may be divided roughly into two kinds; physiologic and pathologic. Physiologic calcification is the normal process which occurs in developing bones just previous to the beginning of ossification. It occurs in a living, healthy tissue. Pathologic calcification occurs in tissues which normally do not contain deposits of this kind, and it is usually preceded by some injurious process in the tissues which leaves them dead or in a damaged condition. It may also occur in old fibrous tissue. The two processes will be studied separately, pathologic calcification being investigated here, and the results of the physiologic process being published in a future paper.

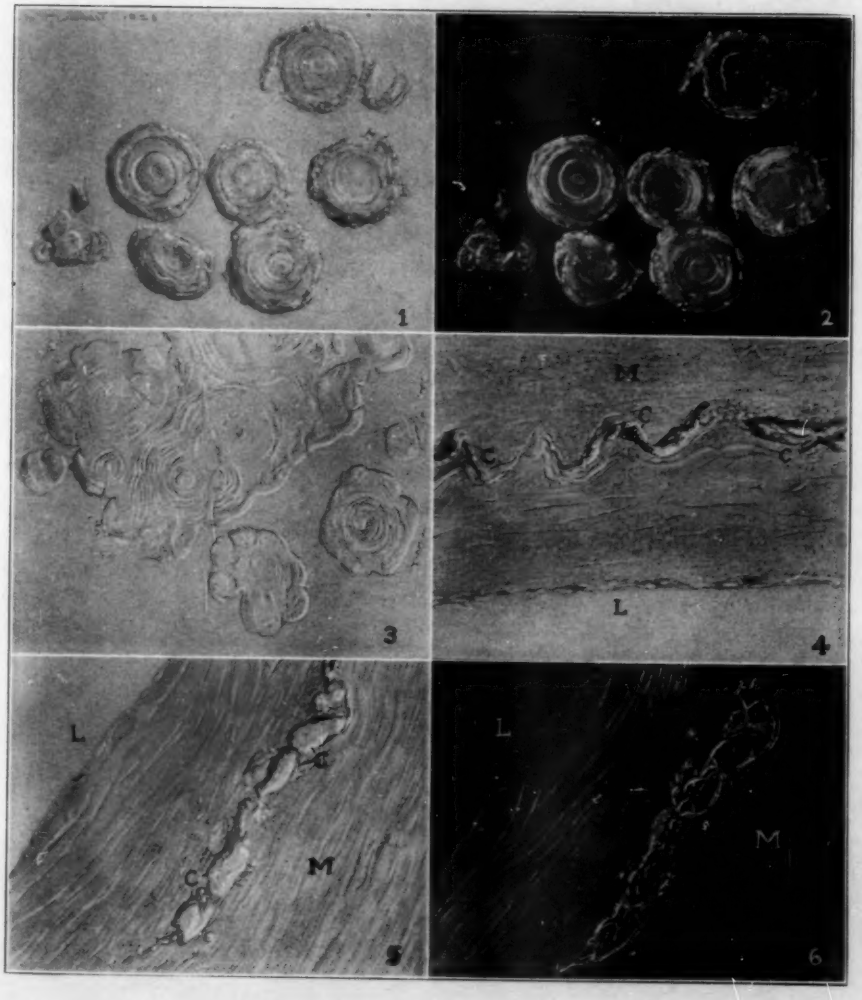
PATHOLOGIC CALCIFICATIONS

Pineal Gland.—Longitudinal sections, 10 microns thick, were made of a pineal gland. It was thickly set in its distal portion with small hard masses which gave a gritty sensation when cut. Microscopically examined, these masses were very noticeable, as they were intensely stained with hematoxylin (fig. 7), and it was found that sections had to be stained lightly in order to show any detail. The deposits varied in size from minute spherical bodies, 1 micron in diameter, up to single bodies from 8 to 10 microns in diameter. Bodies of a larger size ranging up to 150 microns were seen, but these clearly indicated that they originated from a fusion of several smaller masses. In unstained sections (fig. 3) the calcified areas appeared as glassy, crystalline masses. On close examination many of the areas showed a shading in their interior which was much darker in the center, while some, which exhibited concentric rings, gave indications of being laid down in layers.

The appearance of the deposit was strikingly similar to that of spherules of calcium carbonate and phosphate precipitated in a colloidal medium, as shown by the dark center, concentric layers, clear glassy appearance, round spherical form and a tendency toward fusion into large masses.

In some places a definite fibrous wall seemed to surround the deposits completely, but in other cases the glandular tissue was in direct contact with the deposit. No cellular structure was in any way visible in these calcified areas. Specimens were decalcified, and when this was done only the colloidal matrix remained in which the calcium salts were deposited. The matrix appeared homogeneous and reproduced accurately, like a mold, all of the features of the calcareous areas, the

PLATE 1



Explanation of Plate 1

These six figures are from drawings by Miss M. T. Wishart, artist of the Faculty of Medicine, University of Toronto. The drawings are from camera lucida tracings.

Fig. 1.—Deposits of calcium in the form of spherites in the choroid plexus of the descending horn of the lateral ventricle. The specimen was unstained and the fine tissue of the plexus was invisible with ordinary lighting; × 80.

Fig. 2.—Same as figure 1, seen with dark-field illumination. The tissue of the plexus is faintly indicated especially in the lower part of the figure; × 80.

Fig. 3.—Unstained specimens of pineal gland, glandular tissue invisible, calcium spherites shown with indications of their formation by fusion of smaller bodies; × 80.

Fig. 4.—Section of wall of brachial artery, unstained, showing commencing calcification just internal to muscular layer; calcium in masses of granules and irregular fused lumps. In this figure and in figures 5 and 6, *L* indicates lumen of artery; *M*, muscular layer; *C*, deposits of calcium; × 160.

Fig. 5.—Section of wall of femoral artery unstained, showing calcification just internal to muscular layer; × 120.

Fig. 6.—Same as figure 5, with dark-field illumination; × 80.

indications of concentric layers and the lines of fusion of contiguous deposits to form larger masses being clearly visible.

Dark-field illumination of unstained sections showed that the calcified areas were clear and glassy and crystalline in appearance, while the surrounding tissues had only a fraction of the brightness shown by the deposit. Examination with a polarizer showed that some of the deposit was doubly refracting and therefore definitely crystalline in nature.

It may be taken as proved that the masses in this pineal gland were a deposit of calcium because of the following facts: (1) the deposit had an intense affinity for hematoxylin; (2) the appearance of the deposit resembled that of calcium salts precipitated in a colloidal medium; (3) decalcification occurred under appropriate treatment leaving the organic matrix in which the deposit occurred as an excellent replica, which, however, showed different staining reactions; (4) the masses were of all sizes, and the large ones showed many evidences of fusion and fracture in layers and along lines indicating these fusions; (5) some of the deposits showed the behavior of a crystal to polarized light.

The composition of the mass was demonstrated by microchemical means. By the addition of strong acids, such as hydrochloric, effervescence was seen on the unstained sections, showing the presence of carbonates. A dense amount of phosphate was demonstrable by the silver nitrate reaction. By means of the prussian blue reaction, iron was proved to be present in the crystals, but not in such quantity as to be the main part of the mass. Eaves and others have shown iron to be commonly present in calcified areas in the central nervous system, and it is certainly present in this case in a fair amount.

That the process of deposition was by simple precipitation is evidenced also by the facts already enumerated, which are identical with the observations in experimental precipitation in colloidal mediums. This is further proved by the absence of any cellular content in the deposits, such as would be capable of laying down calcium by its secretory activities. In some areas, the pineal cells appeared to be in direct contact with the calcified areas, but it is inconceivable that they could have had any power in forming the area.

Similar deposits of calcium are described by Eaves, who shows illustrations for masses found within the brain which are much like mine.

Choroid Plexuses.—Sections of choroid plexus were examined from the roof of the third ventricle of the human brain, and also from the body and descending horn of the lateral ventricle. These plexuses contained numerous fine nodules which appeared calcareous, and on section were proved to be so. The areas of deposit stained intensely with hematoxylin, many showed concentric layers, examples of fusion were common, and great variation in size occurred, but there were no masses of such size as those seen in the pineal gland.

Mallory's stain colored the calcified areas blue, and after decalcification, the organic matrix of many of these areas appeared orange yellow. Dark-field illumination of unstained sections (fig. 2) showed the deposits as bright, shining, crystalline areas standing out sharply. When these areas were tested with polarized light they were found to be doubly refracting.

The calcium in the choroid plexus in the descending horn of the lateral ventricle appeared as irregular shaped masses (fig. 10) of closely packed granules, the edges of the masses being wavy and irregular in contour and showing distinctly the granular character. Many fine granules were found scattered about where some of these masses had been broken in cutting the sections, and it is certain that these were not stain deposits, as they were exactly similar to the granules seen in the clumped masses of precipitation, and they were not found in any other part of the sections except in the broken calcified areas.

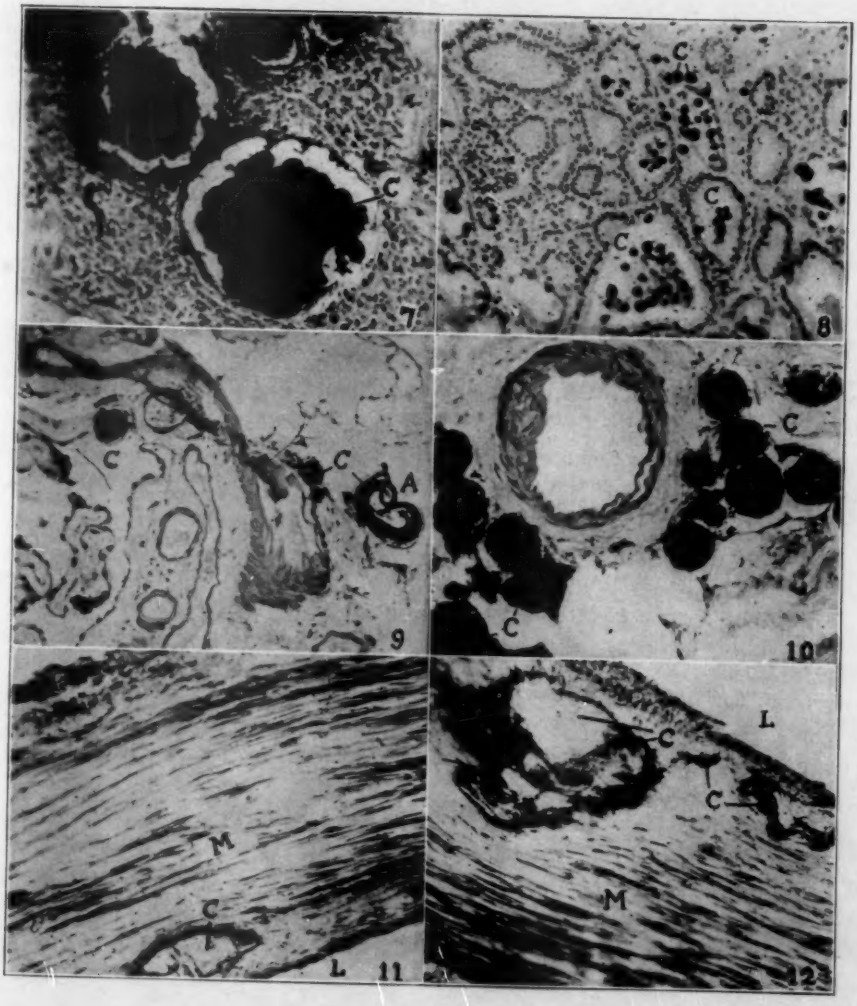
The deposits in this specimen showed areas of calcification commencing as a clumping of five or six small granules. The deposit, evidently caused by precipitation, was not intracellular nor in any special locations, but seemed to occur haphazardly. The larger masses produced by the aggregation of granules here showed imperfect fusion, as the small granules seemed to retain their individuality instead of the whole mass becoming one large crystal. The areas looked as though they would crumble easily into their original granular constituents if crushed.

A second specimen (fig. 9) from the roof of the third ventricle had the appearance of having all its calcified areas contained in blood vessels. Cross-sections showed circular areas with the deposit in concentric rings, the whole area being surrounded by a dense fibrous wall. Sometimes such an area is seen in longitudinal section as a long calcified column in a fibrous wall. Occasionally the fibrous wall is also included as a densely calcified part of the deposit. Two or three such areas showed fractures on cutting, and here the calcified wall had split into layers (fig. 9) in such a way as to suggest strongly its original character as the wall of an artery. The evident assumption was that calcification followed thrombosis in the plexus. The fine granular nature of the deposit was sometimes evident, but fusion into the large masses was much phosphate and a fair amount of iron combined with the calcium.

Microchemical methods showed the presence of little carbonate, much phosphate, and a fair amount of iron combined with the calcium. The carbonate was much less in amount than that found in the pineal gland.

Thyroid Gland.—In the thyroid gland which was examined calcification was diffuse and widespread. In sections stained with hematoxylin, dark blue bodies, often several times the size of a cell, were seen in

PLATE 2



Explanation of Plate 2

Photomicrographs of specimens stained with hematoxylin and eosin. Photography with use of Wratten color filters, done by Mr. W. C. M. Scott.

Fig. 7.—Section of pineal gland showing large calcified masses, *C*, intensely stained; irregular contour of masses gives evidence of their formation by fusion of smaller spherules; × 60.

Fig. 8.—Section of thyroid gland showing densely stained spherules of calcium, *C*, lying in the colloid of the gland; × 60.

Fig. 9.—Section of choroid plexus from roof of third ventricle showing calcified masses, *C*, apparently in blood vessels; and at *A*, the calcified wall of an artery, fractured in cutting the section; × 60.

Fig. 10.—Section of choroid plexus from descending horn of lateral ventricle showing calcified masses, *C*, some with edges showing granular nature; × 60.

Fig. 11.—Section of arterial wall showing small crystalline calcium deposit, with only the periphery stained, and the center clear, at inner edge of muscular layer. *L*, indicates arterial lumen; *M*, muscular layer; *C*, calcium deposits in this figure and in figure 12; × 60.

Fig. 12.—Section of arterial wall with larger calcified area with central clear area and stained peripheral region, also two small areas of calcification densely stained; × 60.

aggregations inside the colloid in the follicles. Examination of the unstained sections with the dark field and also with the polarizer showed that these bodies were clear, glassy, doubly refracting crystals (fig. 8).

Many of these small crystalline deposits were round, but others appeared as triangular and quadrilateral plates, such as those which occur in experimental precipitation of calcium carbonate in colloids. Occurring as these bodies did, embedded in the colloid of the thyroid gland, the interpretation of their presence is that they were formed by precipitation, and their shape indicated that as in the case of the pineal gland their constitution might be almost entirely calcium carbonate.

Arteries.—Various arteries such as the radial, ulnar, anterior tibial and femoral were sectioned through calcified areas which were not too thick and heavy. In spite of this, some sections broke into many fragments, while all were broken in some place or other. These fractures were often of benefit, however, by showing the way in which cleavage occurred in the calcareous masses, and much information could be gleaned from them.

The calcified areas were situated either just under the intima or else in the muscle layers, and varied in size from large masses a third of the circumference of the vessel down to minute spots whose diameters were only a few microns.

The calcified material showed the same features as noted in the case of the pineal gland and the choroid plexuses. Dark-field illumination of unstained specimens brought to view brightly lighted, clear, glassy, crystalline masses, doubly refracting when tested with polarized light. Stained sections showed intense affinity of the calcified area for hematoxylin (figs. 4, 5, 6, 11 and 12).

Some areas appeared to contain the calcium salts in densely packed masses of granules which were shown in clouds at fracture lines where the edge of the mass had crumpled. Other areas were more definitely crystalline and where fractured, plates were split off in the form of triangular and quadrilateral crystals. These areas appeared to be the smoothest, and were usually large and therefore presumably older than other deposits. Some calcified regions appeared under the microscope as dense masses of material laid down in layers which seemed lumpy and uneven, and looked as though they had been formed by the close packing and fusion of rough spherical bodies. Such an appearance I have seen previously in calcium salts precipitated in albuminous solutions.

A peculiar fact noted in connection with the arteries was that in areas showing large calcified masses (figs. 11 and 12) only the periphery of the mass was densely stained with hematoxylin. The remainder of the deposit, centrally placed and therefore older, was either only lightly tinged in color or else was entirely unstained. The unstained portion

looked in every way like a pure crystal, and was evidently in a form which had small affinity for hematoxylin. The newly deposited, more granular peripheral layer of the mass was of recent deposition, and its intense affinity for the stain recalled the madder experiments on bone, in which madder does not stain old bone, but does stain newly formed bone intensely. In the latter instance, Macklin has shown that this staining is due to the calcium which is being laid down in the bone at the time, forming a calcium lake with the madder dye. This intense staining is in line with the reaction which is seen in calcifying cartilage, in which the calcified portion is most intensely colored by the hematoxylin, and here of course the calcium is recently deposited.

In the crystals in the arteries, as time goes on there must be some reorganization in the crystal structure which changes its affinity for stains, recent deposits taking on the colors with avidity, old deposits being inert to them. This is in conformity with examples of reorganization in the crystals which I have described in a previous paper on experimental precipitation of calcium salts in colloids.

COMMENT

There are three aspects of the problem of calcification to be considered, namely, in what form calcium is transported to the tissues where it is deposited, under what conditions it is laid down, and by what means it is thus laid down.

Concerning the form in which calcium is carried in the blood there is no uniformity of opinion, but three fairly closely allied views may be considered as showing the possible ways in which this salt is transported. Pauli and Samec showed that in a colloidal albuminous solution, calcium carbonate and calcium phosphate are many times more soluble than in water. It follows that a reasonable amount of these salts could be carried thus in the blood practically in the form in which they will precipitate.

Holt, La Mer and Chown have demonstrated that blood serum is normally saturated up to 200 per cent with neutral calcium phosphate, and that this salt will remain for days without precipitating. They do not believe that most of the calcium is transported thus, however, but think it is carried as much more readily soluble acid carbonate and acid phosphates which may be converted into the neutral salts by loss of carbon dioxide.

From the latter view to that of Barillé is but a short step. He believes that calcium is found in the blood as a double salt, calcium carbonophosphate, unstable and soluble only in the normal blood concentration of carbon dioxide. If the carbon dioxide content is anywhere reduced, this unstable calcium carbonophosphate dissociates into its two constituents, which further are converted into the neutral carbonate

and neutral phosphate in the proportion in which these salts are found in bone.

Wells has found this proportion of the two salts in bone fairly constant, approximately 15 parts by weight of calcium carbonate to 85 parts of calcium phosphate, or in the proportion of one molecule of carbonate to three of phosphate. He also states that in numerous areas of pathologic calcification the calcium salts are the same as in bone and in the same proportion.

The truth of any of these views cannot yet be accepted as definitely demonstrated, and yet the problem is most important as affecting our views as to the manner of deposition of calcium salts in the tissues, both in the normal process of bone formation and in the pathologic processes of calcification in various tissues.

It will be noted that there are several significant relationships shown in the pathologic deposits of calcium described in this paper. First, it is to be noted that the deposit is not associated with any one type of cell but occurs in many different tissues; second, there are no living cells included anywhere in the masses, such as are seen in the case of bone; third, there is no definite cellular membrane surrounding the mass to which its origin could in any way be ascribed; fourth, the masses of calcium are not even encapsulated or sheathed by fibrous tissue as though there was any tissue reaction to them.

The inference from the conditions just cited is that cellular activity is to be ruled out as the active agent producing the deposition of calcium in these cases. The only process of deposition left, therefore, is that of precipitation. If it is a process of precipitation, it ought to show the characters of the precipitation of calcium carbonate and phosphate in colloidal solutions, as shown originally by Rainey, and later by Harting, Biedermann, Watt and others. This is exactly what is shown, for the various forms peculiar to this process, such as spherules of various kinds, masses formed of irregular crystals, clumps of granules and a marked tendency of bodies thus formed to fuse, are found in the tissues studied. These forms are all characteristic of precipitation of calcium carbonate and phosphate in colloidal solutions, and lead inevitably to the conclusion that they were caused by the process of precipitaton.

Views also vary as to the manner in which precipitation occurs in calcareous areas. A special affinity for special tissues, notably certain connective tissues, has been suggested, but in the present state of knowledge the suggestion has little meaning. Soluble salts reacting with carbonate and phosphate radicles in these locations does not explain why calcification occurs here and not elsewhere, and the supply of phosphate in such locations often seems insufficient.

The most logical explanation for precipitation is that put forward by Barillé, Wells and others that those calcium salts contained in solu-

tion in the blood and tissues are soluble only because of a fixed content of carbon dioxide in the solutions. If the amount of carbon dioxide is decreased, the salts precipitate. It can readily be conceived that in places of low grade activity, like necrotic areas, regions of fibrosis, thrombosed vessels and the colloid in the thyroid gland, there is probably little carbon dioxide; any fluids infiltrating these areas will have their concentration of carbon dioxide reduced, and their calcium salts will precipitate.

For certain areas of necrosis, particularly those in the walls of arteries, Klotz has advanced the idea that soluble sodium and potassium salts in the blood and tissues react with the fatty acids of the necrotic areas to form soaps, and by the reaction of soluble calcium salts with the soaps, insoluble calcium soaps are precipitated. In process of time, by the constant exposure of the soaps to the influence of carbonate and phosphate in the body fluids, a gradual conversion of the calcium soaps into carbonate and phosphate of calcium is accomplished. Klotz has demonstrated the presence of the fatty acids in the necrotic areas, and his ideas are given support by the conditions I have found in arterial walls, where the small, newer deposits, and also a few larger ones are granular, as one might expect the calcium soap to be. Older deposits are definitely crystalline and hard, this change of state agreeing with Klotz' idea of the gradual conversion of the calcium salts formed with the fatty acids into compounds of carbonate and phosphate. This change also explains the difference in staining between the center and the periphery of the large calcified masses in the arteries, where an intense blue is taken by the newly deposited peripheral layer with hematoxylin, but the center remains clear and unstained.

SUMMARY

Areas of pathologic calcification were studied on human material from the pineal gland, the choroid plexuses of the lateral ventricle and third ventricle, the thyroid gland and various arteries.

The deposits were shown to be calcium by their optical appearance in unstained sections and their reaction to polarized light, also by staining reactions, by their removal by acids and by the similarity of their appearance to that of calcium salts precipitated in colloids.

There is no evidence of any cellular activity concerned in the deposition of the calcium salts. There is evidence for their appearance here by precipitation.

The precipitation may be originally in the form of carbonate and phosphate of calcium, or may be as a calcium soap formed by reaction with a fatty acid, and later gradually converted into the carbonate and phosphate.

Iron was found combined with the calcium deposits in the nervous system.

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CHRONIC SEMINAL VESICULITIS AND PROSTATITIS

A FURTHER REPORT ON THE RESULTS OF OPERATIVE TREATMENT AND ITS INDICATIONS *

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In reporting a series of cases of about 200 patients operated on in association with Dr. F. W. Smith in 1923, the symptomatology of seminal vesicle disease was classified into three groups with reference to symptoms. The first group included those cases in which pain is the predominating element with inflammatory changes; the second, those cases in which rheumatic symptoms are present, and the third, those cases in which vague local symptoms are pronounced with an accompanying unexplained neurosis. Three years' further experience bears out the value of this grouping as a working scheme. Operative indications may be similarly epitomized, and these three clear and distinct reasons for surgical intervention and drainage may be given: (1) the evacuation of pus, (2) the relief of pain and (3) the removal of hard, indurated fibrous vesicles productive of systemic, prostatic and bladder symptoms.

GROUP I: PAIN AND INFLAMMATORY CHANGES

Infection of the vesicles occurs in practically 40 per cent of the cases of chronic gonorrheal urethritis when the latter becomes posterior. Ballenger and Elder stress the importance of ascertaining whether gonococci are actually present by the examination of a specimen of the semen. It is claimed that a few scattered pus cells are found in the semen when the prostate alone is involved, but a definitely larger number of polymorphonuclear cells are present when there is extensive infection of the vesicles. In chronic seminal vesiculitis, there is a lesser number of pus cells. It is not the inflammation within the vesicles themselves that is to be considered entirely, as the infection is definitely conceded to be a secondary one superimposed on a gonorrheal type. In a series of many cases examined, gonococci have been found present in less than 2 per cent, and then in lesser proportion to some other organism. As in infections elsewhere throughout the body with specific organisms, such as tuberculosis of the lungs, and other conditions, secondary invasion of organisms persists and accounts for the chronicity of symptoms. It accounts also for the acute attacks that occur subsequently, and in almost every case, for the production of pus. Staphylo-

* From the James B. Brady Foundation of Urology.

cocci of various forms—*Bacillus coli, Bacillus proteus, micrococcus catarrhalis* and various streptococci may be present. In one case, *Streptococcus viridans* was isolated. Evidently there is not any particular selective affinity on the part of the gonococcus for the cavities of the vesicles. Amebas have been reported to have been found recently in the vesicles. However, the gonococcus invades the region of the ampulla and the periampulla and the vasa deferentia with the same freedom that it invades the prostate, the prostatic capsule and the fascia. This is of great importance in the solution of conditions referable to the vesicles, therefore, in that purely perivesicular changes occur, varying from small cicatrized areas to large plaques of dense scar tissue. These are continuous with the capsule of the prostate, and constrict the vesicles, rendering them both incapable of emptying themselves and less resistant to infection. The presence of *Bacillus coli* in many of the patients who were examined, is probably due to the fact that this organism, and others as well, travel from the rectum and traverse the intervening tissues. When a habitat in the vesicles is found with adequate culture mediums, a focus is soon established.

Gonorrheal infiltration usually follows the ejaculatory ducts through to the floor of the urethra, and there is practically a complete elimination of the lumen of the ducts. In delivering vesicles in this type of case, the constriction will resist the extreme degree of manipulation necessary to mobilize them, and the organs can be dislodged from their normal position and brought into the wound without their contents being emptied. It is obvious, therefore, that rectal massage is useless, and many patients are worse after massage because the infection within the vesicle is stirred up by manipulation. There are varying degrees of these periprostatic and perivesicular changes. In some patients the several layers covering the prostate are fused and the whole lifts up like a firm leathery cover; in others, the infiltration is scattered and it is impossible to dissect away the individual layers. This infiltration may progress until it extends well up in to the postprostatic space and becomes fibrous in type. There is then a combination of pressure and inflammatory atrophy of the vesicles, and they exist only as two fibrous cords of almost tendinous consistency. Another type may be noted in which from intermittent or incomplete obstruction within the ducts or periampulla region, the vesicles become engorged and distended, with pressure atrophy of the muscle fibers. This process is comparable to that which takes place in distention of the kidney pelvis and the development of hydronephrosis and may continue until the vesicle is almost cystic. In the case illustrated herewith, it may be noted that the dilatation is extreme.

Deep perineal pain, tenderness over the ischiorectal space and extensions of inflammatory processes which in general have had their

inception in a prostatic abscess, present immediate reasons for drainage. Frequently these infections will first extend down into the epididymis, involve the Cowper's glands, extend back to the prostate again and then break through the prostatic capsule. If this type of case is recognized at the outset, a prolonged convalescence can be prevented by perineal section and multiple incisions into the prostate. This is usually sufficient. If the process continues, it is most likely to extend upward and rupture into the superior pelvorectal space. This rupture is accompanied by a definite relief of symptoms comparable to the rupture of the appendix in an acute appendicitis, however, the relief is of longer duration. The temperature then subsides, and the loose areolar tissue of the space fills slowly with pus and drains the infected area about the prostate and vesicles. The rectum is gradually lifted upward and backward and fully a quart of pus collects before localizing symptoms again appear. Heretofore, the infection in the prostate has been under pressure, with obvious pain and temperature reaction. Symptoms again appear in the nature of rectal difficulties. The patient complains of constipation and difficulty in evacuating the stool, although constipation may never have existed before. The surgeon, being accustomed to examining the prostate, feels this, and if unmindful of developments may possibly miss the pathologic condition farther up in the rectum. If the rupture has occurred around the margin of the base of the prostate where Dénonvillier's fascia dips back to enclose the vesicles, the bulging rectal mucosa may be noted. Generally, however, a proctoscopy will confirm the diagnosis.

Case 1.—G. W. B., aged 36, married, was admitted to the United Hospital, Portchester, complaining of pain in the suprapubic region. He had slightly increased difficulty in urination and his temperature was 102 F. There was a past history of gonorrheal infection. The patient had married since being infected, and had two children.

Rectal examination showed the prostate swollen and tender. The urine was cloudy and contained pus cells and sediment. The patient was treated with rectal irrigations and routine medical measures for four days, after which time the swelling of the prostate subsided slightly. Two attacks of acute retention occurred, for which the patient had to be catheterized. This was accomplished without difficulty. The temperature continued at 100 F. for several days and then began to show a septic curve, rising to 102 and 103 F. daily. There was less urinary difficulty, and the prostate was not particularly tender, nor did it increase in size. There were considerable loss of weight and general malaise; the blood count was 15,800.

Two weeks after admission the patient began to complain of pain in the sacro-iliac region and some sensation in the right leg. This gradually increased, and on rectal examination there was a moderate fullness posterior to the prostate. Rectal irrigations were again instituted, but the swelling increased, extending down to the sulcus to the right of the prostate. A slight tenderness could be made out over the right ischiorectal space.

Diagnosis of prostatic abscess was made, and it was decided to operate. A perineal incision was made, and the prostate was exposed in the usual manner. The posterior capsule was stripped away and the dissection carried up posterior to the seminal vesicles, where a large abscess containing fully 10 ounces of pus was evacuated. From this point, the finger could be carried laterally to the abscess cavity as it was carried forward into the right ischiorectal space; the areola had been entirely destroyed. The superpelvo-rectal cavity was drained directly, and a counter drainage was established through the ischiorectal space. The patient made an uneventful recovery, and has been well since that time. When recently heard from his condition was good.

GROUP II: RHEUMATIC SYMPTOMS

Rheumatism is the principal symptom associated with chronic vesiculitis. In this connection the following characteristic of posterior infections may be noted. If there is a complication with an original urethral infection, the same complication is likely to occur with subsequent attacks. For example, if from five to ten days after the onset of a urethral infection epididymitis develops, the same complication will occur in subsequent infections. This is also true when joint symptoms occur. If there is a recurrence, as is likely in 90 per cent of the cases, or if there is another attack, it will be accompanied by a return of the rheumatic symptoms. This early development of complications signifies one of two important clinical facts: the infection is a severe one, or resistance is not great. In almost 95 per cent of the cases of gonorrheal rheumatism, the latter is true. As rheumatism is seldom seen as a complication in private cases, but rather in hospital cases, usually in the municipal hospitals, the problem takes on an economic aspect. What is the best method of reducing the hospitalization time of these patients, provided that it does not detract from the efficacy of treatment for the original condition?

The answer to this is prostatotomy and seminal vesiculotomy. This not only cuts down the time of the first attack, but lessens the incidence of an associated rheumatism with subsequent attacks. The focus of infection within the prostate or vesicles, if isolated by circular inflammatory changes and scar tissue as described above, acts as definitely as diseased roots or apical abscesses in causing rheumatic joint symptoms.

GROUP III: LOCAL SYMPTOMS AND NEUROSIS

The third group of cases may be attributed to inflammatory changes that have extended backward and involved the trigone and neck of the bladder. The infection extends to just beneath the mucosa, with involvement of the muscles of the trigone. This may give rise to various disorders of urination, such as a sense of incomplete emptying, difficulty in starting the stream and tenesmus. There may even be perineal pain and a sense of fulness in the perineum and at the neck of the bladder. The patient may say that the neck of the bladder feels stiff after urinat-

ing, as if the bladder wall could not fully contract. This is due to stiffened, unyielding vesicles which extend out onto the bladder wall like a pair of brackets converging to the vesical neck and adherent to the bladder wall. One author reports a case in which extravasation occurred at the site of the vesicles and extended forward along the usual fascial plane, and it was only in radical incision of the perineum that he noted the opening in the bladder at this point. He cites the possibility of this factor being present in other cases of extravasation, and states that abscess formation in the vesicles with destruction of tissue together with a firm stricture anteriorly may account for the extravasation. The cystoscopic examination reveals a well defined trigonitis in many cases, and occasionally the outline of the distended vesicle can be seen showing through the bladder floor. Injected vessels in an area limited by the outline of the vesicles have occasionally been noted. The results of the cystoscopic examination are confirmatory, however, rather than absolutely diagnostic, and serve to explain the bladder symptoms frequently found and mentioned by numerous investigators.

The factor of chronic vesicle inflammation in impotence is a difficult one to judge. It would seem that infection of the vesicles exists in at least 65 per cent of the cases of impotence; however, it does not follow that this could be cured by operation. This eliminates a large number of so-called neurotic cases, in which the so-called "sexual neurosis" of the patients is attributable to chronic vesicle infection. Interference with the nerve supply as a result of the perivesiculitis, together with a lessened capacity of the vesicles, accounts for the impotence and associated symptoms of which these patients complain. It is true, however, that cures or even relief can be expected to a lesser degree in this class of cases than in any other, and operation may make their condition worse.

It might be noted that as a factor in persistent discharge vesiculitis plays an insignificant rôle, and reference to the tables will readily demonstrate this. Twenty-two cases were seen with a view to operation for persistent discharge; leukocytes were found; the duration of the condition was more than a year. Seven cases were considered suitable for operation. Five patients showed a marked degree of improvement sufficient to justify the procedure; two were slightly improved. An operation should never be considered in these cases until massage has been tried. It may be that the retention within the vesicle is due to the pressure of a distended and boggy prostate on the ducts. If, however, extensive inflammatory and suppurative processes have existed, it is probable that the ducts are stenosed and the symptoms thereby aggravated. However, massage often gives satisfactory results. The following case is illustrative.

CASE 2.—C. C., admitted to St. Bartholomew's Hospital Clinic, had been treated three years before for gonorrheal infection which was accompanied by a severe prostatitis and posterior urethritis. Irrigation and the usual measures of treatment were used, under which discharge subsided. One year after the original infection, the patient developed a pain in both knees, which made it necessary for him to discontinue work. At times he walked with the aid of a cane. Further examination showed the prostate markedly distended and hard; this disappeared on vigorous massage, followed by rectal irrigations. The patient said that there was immediate relief of symptoms following massage. Gonococci were demonstrable in material obtained from prostate. Following the lessened presence of pus cells in the secretion, the ejaculatory ducts were catheterized and irrigated with 1 per cent solution of mild silver protein. A marked

TABLE 1.—*Symptoms and Treatment in Series of Cases Discussed*

Cases		Average Duration	Treatment	
			Operative	Palliative
19	Acute arthritis	5 weeks	11	8
11	Chronic arthritis	6-9 months	11	..
19	Urinary disturbances	5 months	7	12
27	Chronic discharge	1 year	7	20
9	Dysuria	6 months	2	7
11	Impotence	?	..	11
4	Right-sided and left-sided pain	6 months	2	2
6	Epididymitis	6 months	4	2
7	Pyuria	?	5	2
2	Acute retention	.....	0	2

TABLE 2.—*Results of Operative and Palliative Treatment*

Operative				Palliative		
Cured	Improved	Unimproved		Cured	Improved	Unimproved
9	2	..	Acute arthritis	..	2	6
9	2	..	Chronic arthritis	..	..	..
4	1	..	Urinary disturbances	..	8	14
5	2	..	Chronic discharge	2	13	5
2	..	..	Dysuria	..	3	4
..	..	..	Impotence	..	..	..
1	1	..	Right sided and left-sided pain	..	1	1
3	1	..	Epididymitis	..	1	1
4	1	..	Pyuria	1	1	..
..	..	..	Acute retention	..	1	1

improvement was noted, and four months after the beginning of the treatment the joint symptoms had disappeared entirely. It was noted that the edema of the ejaculatory ducts which was present at first had entirely disappeared, and a bougie could be passed without pain. Roentgenograms of the joints did not show prominent joint changes. Three years after treatment the patient was still free from pain.

In some cases a bougie or fine sound passed into the ducts through a urethroscope is effective in reestablishing drainage. This measure should always be utilized and is most useful when patients complain of deep-seated pain after coitus; when the pain is due to stricture of the ejaculatory ducts, dilatation often brings about a relief of symptoms.

Seminal vesicle disease should be borne in mind, likewise, in conditions of the upper genito-urinary tract when ureteral obstruction is

evident. Ureteral stricture due to extrinsic causes—periureteritis, and other conditions, often results from infection elsewhere in the body. Infected teeth, root abscesses and diseased tonsils are ready sources of origin. Less remote is the extension of infection from the adjacent vesicles. The relationship of these structures is marked. The process is periureteral, and infiltration of the ureteral wall is not present. In cystoscopic examination in these cases, the orifice on the affected side will be noted as occupying an abnormal position. It is usually pulled externally as the contraction seems to extend in that direction rather than toward the midline of the bladder. Cystoscopy likewise often gives a direct clue to the nature of the infection. In the injected and congested trigone, the outline of the vesicle can be noted through the mucosa, and in well defined cases the vascular outlines follow more or less accurately the shape of the vesicle. Cystoscopy should not be overlooked, therefore, in attempting to arrive at a diagnosis, and any abnormality in the position of the ureter should be noted. In strictures and narrowings just above the orifice, the vesicle should be examined.

In tuberculosis of the lower tract, the disease is likely to extend to the ureter when once the prostate and vesicles have become involved. In this case the ureteral constriction is more marked. The cystoscopic changes are characteristic, but the infiltration of the ureter often makes it impossible to catheterize the ureter. The infection spread from the tissues and fasciae around the vesicle, anteriorly and involves the muscle of the bladder. Considerable resistance is offered at first, and there is a tendency for cicatrization and involvement of the trigone and orifice. It would seem that a tuberculous ulceration might occur, but this is never seen. The process involves the ureter, infiltrating first the muscular layer. Edema of the mucosa occurs, but slowly, apparently, as there is never a history of renal colic. Finally, a small channel remains in the ureter through which the kidney can excrete. It is impossible to introduce the finest bougie into the ureter. The mucosa is easily traumatized and bleeds, and after one attempt it is impossible to try again for three or four weeks. Tubercle bacilli are seldom found, and, if present, one cannot be certain that they have not come from the kidney into which there may have been further extension. Usually a firm scar forms with retraction of the orifice upward and backward. Its real position is easily recognized, and with one finger in the rectum, palpating the vesicle, and the cystoscope in position, the orifice can be seen to move as if it were a part of the vesicle itself. I have seen seven such cases.

Case 3.—A man, aged 32, married, complained of loss of weight, marked discomfort in the perineum and at the neck of the bladder, together with nocturnal frequency. Two months before he consulted me, he had noted marked increase in nocturnal emissions, at one time he averaged one a night.

The left epididymis was slightly increased in consistency, but nodules were not made out. The left seminal vesicle could be palpated as a definitely indurated prominent stricture in the postprostatic space; it was moderately tender. A preliminary diagnosis of tuberculosis of the seminal vesicle was made, and the patient was advised to have cystoscopy performed. This was done the following day. A marked trigonitis was found with injection in the region of the left vesicle; the left orifice was pulled upward and outward, and an attempt to pass a ureteral catheter was followed by rather free oozing. Several types of catheters were tried without success. The patient did not have a reaction for three days, when a marked left epididymitis developed. He went into the hospital for one day, and the pain and swelling subsided. A specimen of the urine which was injected into a guinea-pig was reported negative. Three months after examination the patient was seen again. Two small nodules were present in the left epididymis, and the vesicle was still tender and swollen. The patient's bladder had been irrigated twice a week during the interval. It is probably that this reduced the changes near the ureteral orifice, but the patient would not allow this to be confirmed by cystoscopy.

Diagnosis of tuberculosis of the right vesicle, quiescent in type, seemed unquestionable, and was confirmed by a consultant who also saw the patient.

CASE 4.—D. F. D., aged 23, unmarried, complained of frequency of urination and a sense of fullness in the perineum and occasional swelling of the left testicle and the epididymis. Both vesicles were palpable, the left more so than the right, and distinctly swollen and tender. The patient complained also of pain in the region of the left kidney, and the organ was slightly enlarged and lower than the opposite kidney. Cystoscopy showed an injected trigone and neck of the bladder; the ureteral orifice was elevated and pulled upward and inward. It was impossible to catheterize it, although attempts were made on more than ten different occasions. An injection of indigo-carmine showed a return two minutes later in the opposite side and a dye issue in a fair sized swirl.

Diagnosis was made of left tubercle seminal vesiculitis, localized, with tuberculous stricture of the ureter. The patient was observed for two years, but has since disappeared from observation.

Young has reported good results in the treatment of tuberculosis of the lower tract, epididymis, vas and vesicles by removal of the organs en masse. His results are unusual, however, and generally much improvement cannot be expected. This process is as likely to be cured under hygienic treatment as by operation. Difficulties are encountered at every stage; the possibility of spreading the infection within the inguinal canal is not remote, urethral fistulas are not uncommon, and the perineal wound heals with difficulty. When palliative measures, as recommended, have been given a fair trial, a perineal operation with the exposure of the vesicles and removal or thorough drainage is indicated.

OPERATIVE PROCEDURE

The patient should be in the so-called exaggerated lithotomy position, described by Young, as the operative procedure is much facilitated. The sacrum is elevated from the plane of the table and the buttocks brought out over the edge, which brings the perineum almost parallel

with the floor—a great advantage in all perineal procedures. A curved incision is then made starting from the ischial tuberosities and continuing through a point which is just superficial to the termination of the bulbous urethra. This point can be determined by palpation of the perineum on a sound which has previously been placed in the urethra. The central portion of the incision should be carried to a depth of at least 0.5 cm. This measure is important, as it provides for better healing

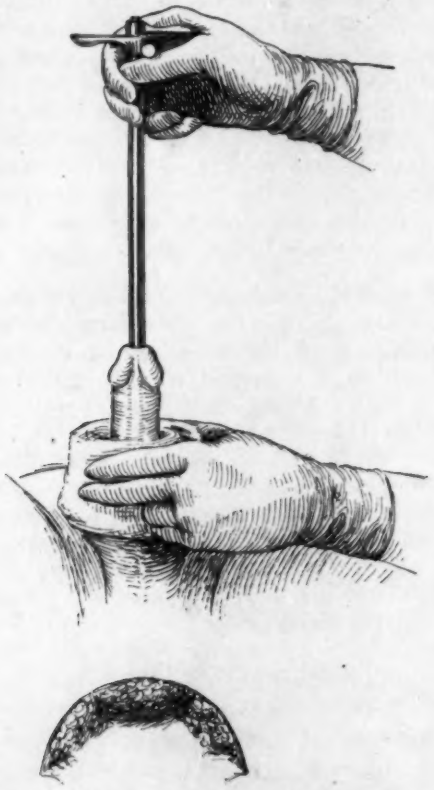

Fig. 1.—Seminal vesicle tractor in position and line of incision. This incision is carried much deeper in the center than at the sides, and the upper angle of the wound corresponds to the junction of the bulb and membranous urethra. If this precaution is observed, there is much lessened possibility of hemorrhage.

of the central portion of the skin flap. In a large series of cases we failed to obtain a sloughing of the triangular portion at the end, as is often seen when an inverted V incision is made. Retraction of the skin flap exposes the site of the central perineal tendon; the tendon is divided sharply after blunt dissection of the lateral fossae on either side. At this point it is important to proceed carefully and retain all the fibers of the bulb in the upper portion of the wound. The thin

fibrous line of the central tendon, as it converges toward the bulbomembranous junction, can be plainly seen. This prevents a great deal of bleeding from the vascular bulb.

The sounds should then be removed from the bladder and a seminal vesicle tractor inserted (fig. 1). Traction on this pushes the prostate forward and elevates the apex. By careful sponge dissection after previous introduction of the finger into the rectum, it is possible to strip away from the apex of the prostate the well defined attachments of the recto-urethralic muscle. At this point the muscle becomes prominent, and it is necessary to guard against injury to the rectum. In observations on numerous operations in which the rectum has been injured, precautions regarding the rectum are usually taken prior to this time, since here the rectum and prostate are in close relation.

Figure 2

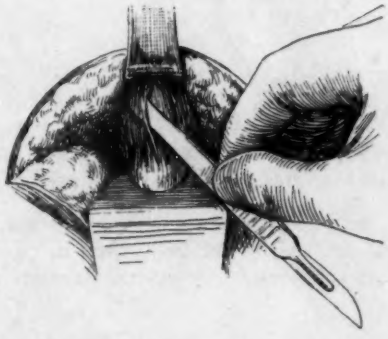

Figure 3

Fig. 2.—Division of the superficial transverse muscle of the perineum with exposure of the recto-urethralis and the deeper structures.

Fig. 3.—Elevation of the muscular layer of the recto-urethralis from the urethra and apex of the prostate.

Gentle tension on the flap with one finger in the rectum stretches these fibers, and they can be divided with the scissors close to their insertion in the urethra (fig. 2.) When the rectum has been separated from over half of the anterior surface of the prostate, the remainder of the procedure can usually be accomplished by gauze dissection. The free edges of the levator ani at this point come into view, and they can be lifted gently from the posterior surface of the prostate and separation continued by hooking the finger under the free edge of the muscle and further detaching it, after which it can be retracted from the wound (fig. 3).

The posterior surface of the prostate now comes into view, and this should be cleansed of a few adherent fibers (fig. 4) of muscle tissue and other débris which have remained from the removal of the rectal wall. This is best accomplished by the handle of a knife, and the white capsule

of the prostate is distinguished by its fascia-like character. The prostate is then retracted firmly into the wound and an incision made transversely, at a point just behind the middle axis of the gland. Numerous engorged blood vessels, the latter the result of the vesicular infection, frequently can be noted in the tissues, and the incision can be varied to avoid these. If sectioned, they give rise to troublesome bleeding. At this point care should be taken to recognize the existence of a special fascial plane

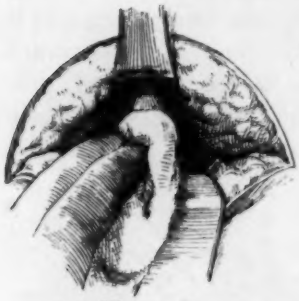

Figure 4

Figure 5

Fig. 4.—Stripping off the fibers of the recto-urethralis with gauze sponge and beginning exposure of the apex of the prostate.

Fig. 5.—Elevation of the prostate into the wound by means of the tractor and division of the two layers of the prostate fascia which covers the prostate posteriorly and involves the seminal vesicles.

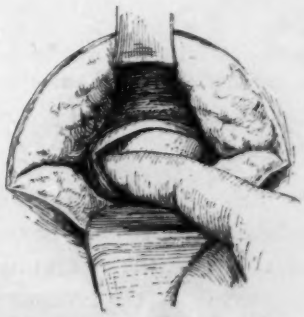

Fig. 6.—After a line of cleavage is obtained, Dénonvillier's fascia can be stripped from the prostate by the index finger.

covering the vesicles, and after division of the first layer of the fascia, a second layer should be identified and stripped back in order to reach the vesicles (fig. 5). The tip of the index finger is then inserted anterior to the fascia and along the posterior surface of the prostate, extending outward, and the vesicles can be palpated (fig. 6). Pressure on the organ will sometimes expel a moderate quantity of vesical contents through the urethra. Enucleation is then begun at the tips of the

Fig. 7.—Removal of one layer of Dénonvillier's fascia and separation of the second layer. If these layers are removed separately, there is less danger of the finger rupturing posteriorly into the rectum.

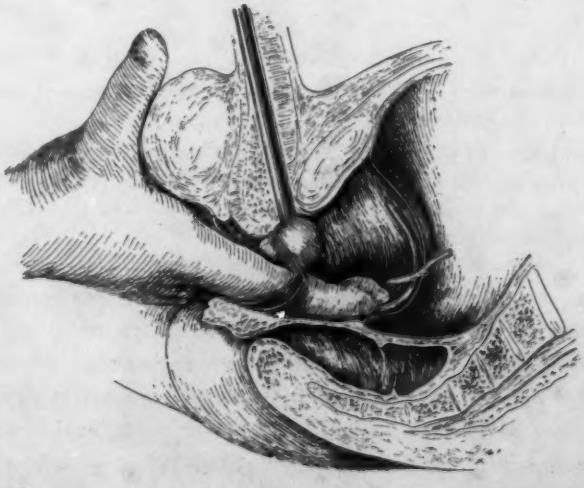

Fig. 8.—Sagittal section, showing the extravesicle and extraprostatic limitations of the enucleation. The finger is carried posterior to the prostate and in front of the two layers of the prostatic capsule to the tip of the vesicle, which, as may be noted, lies just before the point at which the ureter enters the bladder. There is scarcely any danger of injury to the ureter. Enucleation is carried out by dislodging the tip and finding a line of cleavage between the vesicle and the floor of the bladder. In cases of prolonged inflammation, this may be difficult.

vesicles until they are freed. Numerous adhesions to the base of the bladder are noted, but these can be broken through without difficulty; further adhesions between the vas, which at this point is directed internally toward the ampulla, are likewise separated (fig. 7). A gauze sponge on a holder, if introduced into the postprostatic space, is often of assistance in drawing the entire structure forward, and the rest of the procedure can be completed under the guidance of the eye (fig. 8).

In vesiculotomy, an incision is made in the vesicle at the point where it joins the ampulla, and numerous incisions are made along the axis of the organ. The vesicle is crushed at this point and then excised (fig. 9). The necessity of ligation has not been noted, although

Figure 9

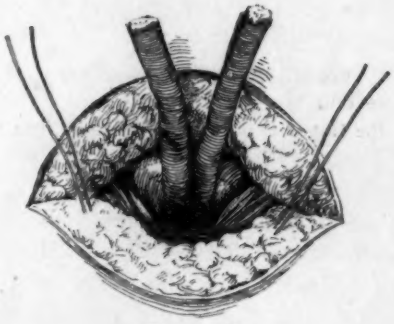

Figure 10

Fig. 9.—Delivery of the seminal vesicle into the wound with clamp in position for left vesiculectomy.

Fig. 10.—Closure of the wound. The drains extend posterior to the prostate; the vesicles after section or removal have been replaced. A heavy suture through the two levator ani muscles serves to obliterate almost the entire cavity. A second suture can be placed superficially.

ligation may be done. It is wise to determine the presence of this secondary layer of fascia. In some operative procedures, the prostate is excised too deeply; and when the finger is inserted posterior to the prostate, the vesicles cannot be felt because, together with their fascial coverings, they have been forced down beneath the level of the finger.

The prostate is incised liberally, drainage tubes or wicks inserted at the site of excision or incision and the prostatic capsule sutured in two places. The sound is withdrawn from the urethra and a loose suture placed in the edges of the levator ani muscle; this is drawn over the prostate, and the central tendon is remitted (fig. 10). Further sutures are not taken, except in the skin, which is closed with interrupted silkworm gut; the tube is brought out on each side of the central portion of the wound.

There is often excessive bleeding, as seen in all other operative procedures on the bulb and the perineum, such as strictures of the urethra, external urethrotomy, etc. The oozing following the separation of the vesicles from the base of the bladder may be considerable. Packing is sufficient to check this, but occasionally the oozing continues, and when the subsequent clot breaks down, convalescence is measurably hastened. If two rubber tubes or pieces of catheter, size 28 to 30 French, are introduced with the packing, the clots may be washed out and irrigation carried on through them for two to three days at most (fig. 11). The tubes may then be removed.

Convalescence is generally uneventful. Before using the tubes in addition to packing, several hemorrhages are likely to occur, and convalescence may be prolonged unduly. This difficulty has now been overcome. Rectal injuries may and do occur. The rectum may be

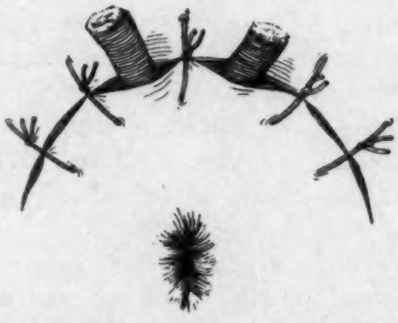

Fig. 11.—Closure of the wound with two cigaret drains extending into the seminal vesicle cavity. This technic is now modified by the inclusion of a catheter introduced together with the wicks for irrigation.

cut or the point of the retractor torn through the wall. All these lesions heal without incident; more than ten or twelve days are seldom added to the period of convalescence.

COMMENT

The specimens removed at operation showed a variety of pathologic changes. Early workers in this particular field determined that the process was almost entirely a perivesicular one, and scar tissue with mononuclear infiltration comprised most of the tissues removed. Dillon and Blaisdell have comprehensively grouped the changes into two classes—those involving the intrinsic structures and those involving the extrinsic processes. In numerous patients operated on, I have noted considerable scar tissue in the prostate. Microscopic sections have shown at times fibro-adenomatous hypertrophy of the prostate.

In these patients the vesicles are usually cystic and greatly dilated. There may be simple engorgement of the subepithelial blood vessels to round cell infiltration of the wall, with formation of granulation tissue and organized exudate which incorporates the tip of the vesicle to the extent that it cannot be freed. In patients in whom the vesicles have been the seat of an inflammatory process, the vesicles are atrophied and form two thickened branches of scar tissue which have lost all semblance of their original anatomic contour. A type similar to this is seen in tuberculosis, but with less atrophy. The tubercle bacillus invades the wall of the vesicle, and infiltration continues at the expense of the cavity, which is finally obliterated. The cavity is filled with an inspissated cellular débris which contains broken-down epithelium, red blood cells and occasionally, if there has been a recent inflammatory process, leukocytes and free pus. It is in this type of case that there will not be any reaction to treatment, and in which improvement must result from operative measures. The accompanying prostatic involvement is of great significance. Free incision of the capsule both laterally and beneath the ejaculatory ducts relieves the hyperemia, and prolonged drainage changes the cellular structure to a degree that the constriction of the ejaculatory ducts is relieved. When the vesicles are drained or removed, the ampulla undergoes a similar change if inflammatory changes persist in the prostate.

In the first group of patients in which pain is the predominating element, there is immediate relief, particularly when a quantity of pus is evacuated. When there is dull, throbbing prostatic pain, regardless of free pus, relief is obtained in the same manner. In cases in which rheumatism is present, pus is evacuated, and the most recent joint involvement disappears. If all joint symptoms have been acute, the pain and swelling quickly subside. If there is inflammation of the knee, greater freedom of motion is soon noted and lessened pain, but the swelling persists. These patients derive benefit from the application of intense heat, which promotes absorption of the exudate. In general, results are most satisfactory.

In the third group, in most cases the results are not as satisfactory. Operative indications cannot be said to be as definite, and surgical intervention is generally employed after a prolonged course of various other forms of treatment. While convalescing, these patients should be treated systematically with irrigations of the bladder and applications to the vesical neck and trigone. It is difficult to follow all of the patients in this way, and this lack of individual attention may explain some proportion of the failures.

CONCLUSION

Infection of the seminal vesicles and perivesicular tissue occurs as a complication of gonorrheal infection, and persists after the original infection has apparently subsided.

Persistent and latent infections of the vesicles give rise to three definite groups of symptoms.

Patients with cases belonging to these classifications should be operated on, and there should be surgical drainage of the vesicles, prostate and adjacent tissues.

Operative procedure, beyond prescribing technical difficulties common to all perineal sections, is not serious, or attended with unusual danger to the patient.

Results, from the standpoint of relief from symptoms, lessened physical disability and shortened convalescence, justify a continued and more frequent use of this method.

HYPERTROPHIC ARTHRITIS OF THE SPINE

ITS INCIDENCE AND NATURE IN PATIENTS MORE THAN FIFTY YEARS OLD *

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In the Section on Roentgenology at the Mayo Clinic the incidental occurrence of hypertrophic arthritis of the spine in middle-aged and elderly persons with other diseases has attracted more than passing interest, and led to this study to determine the incidence and nature of the disease among such patients. The study of incidence was based on the cases of 2,090 patients more than 50 years of age, who were referred to the section for roentgenograms of the kidneys, ureters and bladder during the year 1925. This particular group was selected because in the roentgenogram of the genito-urinary organs the spine is clearly shown incidentally. A suspicion of disease of the spine was not included in the reasons for reference except in a small percentage. Such cases are usually referred explicitly for a roentgenogram of the spine itself. This study of the nature of this disease is based on a detailed analysis of 500 cases showing hypertrophic arthritis of the spine. The chief complaints of the patients on admission, complaints possibly spinal in origin, evidences of senescence, the presence of apparent and possible foci of infection and the incidence of obesity have been considered. Note was also made of the final diagnosis in each case.

INCIDENCE

The incidence of hypertrophic arthritis of the spine, based on the total group of 2,090 cases is shown in table 1. The predominance of men is explained by the large number of cases of hypertrophy of the prostate in the group, as it is a routine procedure at the clinic to obtain a roentgenogram of the kidneys, ureters and bladder before cystoscopy.

DETAILED ANALYSIS

Of the 500 patients selected indiscriminately from the group with arthritis of the spine, 160 were women and 340 were men, and in the analysis the sexes are considered separately as regards presenting complaints, diagnosis, and other factors. The chief complaints of the women in this group are indicated in table 2, and those of the men in table 3.

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* Thesis submitted to the Faculty of the Graduate School of the University of Minnesota in partial fulfilment of the requirements for the degree of Master of Science in Medicine, April, 1926.

The disproportionate number of urinary complaints is due to the large number of cases of prostatic disease in patients more than 50 years of age. The many cases with abdominal complaints in such a group of roentgenograms are explained by the fact that often the presence of an obscure or indeterminate abdominal symptom not clearly related to any viscus will prompt the clinician to refer the patient for roentgenographic examination to determine whether the urinary tract is involved.

TABLE 1.—*Incidence of Hypertrophic Arthritis of the Spine with Other Diseases*

	Total Cases	Arthritis	
		Cases	Per Cent
Men	1,415	939	67
Women	675	271	40

TABLE 2.—*Chief Complaints of Women with Hypertrophic Arthritis of the Spine*

	Cases	Per Cent
Gastro-intestinal and indefinite abdominal disease	57	55.6
Genito-urinary disease	42	26.2
"Rheumatic" and neuromuscular disease	23	16.3
Weakness, nervousness, anorexia, etc.	16	10.0
Miscellaneous: headache, dyspnea, heart trouble, goiter, rectal trouble, edema and diabetes, indefinite	19	11.9
Total	160	

TABLE 3.—*Chief Complaints of Men with Hypertrophic Arthritis of the Spine*

	Cases	Per Cent
Genito-urinary disease	205	60.3
Gastro-intestinal and indefinite abdominal disease	52	15.3
"Rheumatic" and neuromuscular disease	34	10.0
Nervousness, weakness, fatigue, etc.	17	5.0
Indefinite	17	5.0
Miscellaneous: chills, heart trouble, dizzy spells, goiter, palsy, etc.	15	4.4
Total	340	

TABLE 4.—*Incidence of Complaints of Backache, Lumbago or Sciatica*

	Total Cases	Backache, Lumbago, Sciatica	
		Cases	Per Cent
Men	340	89	26.0
Women	160	62	38.7

It will be noted that there were but sixty patients in both sexes with rheumatic, neuromuscular or definite disease of the joints as the chief or presenting complaints. However, the specific complaints of backache, lumbago and sciatica were given as chief or secondary symptoms in a somewhat larger number of cases, some of which are of course included in the general classification as "rheumatic," and so forth (table 4).

It will be seen, therefore, that 74 per cent of the men and 61.5 per cent of the women with hypertrophic arthritis of the spine had no accompanying complaint of the various types of rheumatic and neuromuscular pains. That there should be many patients with definite spinal changes without symptoms is rather to be expected, and has been observed by other writers on the subject. Nissen [1] has noted that the condition may exist for years and give no symptoms until there has been a sprain, a strain, a chilling of the body, fatigue or some other exciting cause. The subjective symptoms, according to Goldthwait,[2] are usually slight in comparison to the actual pathologic change, so the condition is discovered incidentally. Rosenheck [3] comments on the fact that one may see extensive disease of the vertebrae with practically no radicular involvement. Radicular involvement with hypertrophic arthritis of the spine has been noted as a cause of abdominal pain. However, there were no cases in this group of 500 in which pain in the abdomen could be attributed only to the spinal arthritis. Parker and Adson [4] have reported only eight cases seen at the Mayo Clinic from August, 1922, to November, 1924, in which there was definite suffering from a compression of the spinal cord or its roots due to hypertrophic osteo-arthritis of the spine.

In tables 5 and 6 the primary diagnoses in the 500 cases with arthritis of the spine are given in the order of their frequency, those of various pathologic conditions in the genito-urinary tract naturally predominating among both men and women.

Seventy and six-tenths per cent of the diseases of the urinary tract among men are comprised of prostatic disturbances. In addition to the various primary diagnoses of prostatic disease given in table 6, the prostate was involved secondarily as benign hypertrophy in seventy-one, as prostatitis in seven, and as a postoperative condition in two other cases, a total of 253 out of 340 cases in which the prostate was affected.

CAUSES OF HYPERTROPHIC ARTHRITIS

The same three factors that are the cause of disease in general cause arthritis: (1) infection, (2) retrogressive or metabolic changes and (3) irritation, chronic or acute. These three causes may act alone or

1. Nissen, H. A.: Some Observations on Arthritis, M. Clin. N. Amer. **8**: 1789, 1925.

2. Goldthwait, J. E.: Osteo-arthritis of the Spine: Spondylitis Deformans, Boston M. and S. J. **141**:128, 1899.

3. Rosenheck, C.: Radicular Pain and Its Relation to Spondylitis Deformans from a Neurological Viewpoint, M. J. and Rec. **122**:215, 1924.

4. Parker, H. L., and Adson, A. W.: Compression of the Spinal Cord and Its Roots by Hypertrophic Osteo-arthritis; Diagnosis and Treatment, Surg. Gynec. Obst. **41**:1, 1925.

in combination. The classification of arthritis used at the clinic, excluding specific and neuropathic forms, is: (1) infectious (nonspecific), (2) senescent and (3) traumatic.

Infectious, nonspecific arthritis may produce roentgenologic changes of a purely periarticular type, hypertrophic or destructive changes in bone, or atrophic changes in bone and cartilage. This infectious nonspecific type is characterized by its situation in many large joints or in the proximal and middle joints of the fingers, and occurs primarily in adults between the ages of 20 and 40. Cold, clammy hands and hypotension are two prominent symptoms.

TABLE 5.—*Primary Diagnosis in Cases of Women with Hypertrophic Arthritis of the Spine*

	Cases	Per Cent
Genito-urinary diseases: carcinoma of bladder, cystitis, pyelonephritis, cystocele, hydronephrosis, renal stone, urethritis, carcinoma of kidney, urethral caruncle, fibrosis of the bladder, etc.	55	34.4
Cholecystitis, with and without stones	27	16.9
Arthritis	17	10.6
Miscellaneous: myocardial degeneration, chronic nervous exhaustion, migraine, constipation, duodenal ulcer, appendicitis, inguinal hernia, etc.	61	38.1
Total	160	

TABLE 6.—*Primary Diagnosis in Cases of Men with Hypertrophic Arthritis of the Spine*

		Cases	Per Cent
Genito-urinary diseases		240	70.6
Benign hypertrophy of the prostate	120		
Prostatitis	35		
Carcinoma of the prostate	18		
Carcinoma of the bladder	11		
Renal and urethral stones	11		
Miscellaneous: carcinoma of the kidney, pyelonephritis, stricture, tumors of the bladder, cystitis, etc.	45		
Hypertrophic arthritis		20	5.9
Cholecystitis, with and without stones		10	2.9
Arteriosclerosis		13	3.8
Miscellaneous: pulmonary tuberculosis, latent syphilis, diabetes, myocardial degeneration, carcinoma of the stomach, etc.		57	16.7
Total		340	

Senescent arthritis occurs usually in persons beyond middle age, is generally confined to the distal joints of the hands as Heberden's nodes, or to the spine and knee The bony changes are almost always hypertrophic. This type is usually accompanied by mild hypertension, arteriosclerosis and other evidences of senescence.

Traumatic arthritis, acute or chronic, may be a periarthritis affecting only the soft tissues, or also the bone, in which case the bony changes are usually hypertrophic. Examples of this are "baseball fingers" and "static" arthritis, such as are found in obese patients.

It will be seen, therefore, that hypertrophic bony changes are not confined to any one causative type of arthritis, but may occur in several

different types, although the term hypertrophic arthritis is often used to mean exclusively a purely senescent or metabolic and not infectious form of the disease.

The pathologic change seen in hypertrophic arthritis is described by Goldthwait as a proliferation of the edges of the articular cartilage, with subsequent ossification and extension of the process into the ligaments originating nearby.

In elderly persons, such as those under consideration in this series, hypertrophic arthritis may well be due not to one factor alone but to a combination of factors. An analysis of possible causative factors has been made; foci of infection have been sought; chronic trauma, especially in cases of obesity, has been considered, and senescence has been determined by other evidences.

That infection, slight or severe, may play some rôle in the etiology of the type of arthritis under discussion is generally agreed, although the degree and manner of its elucidation are sometimes difficult to determine. Even in cases which at first seem independent of infection there are good reasons for thinking that the microbe factor is contributory. Ely [5] believes that the disease is primarily infectious and that "it is almost exclusively in persons whose alveolar processes have had abscesses at the roots of their dead teeth." Horder [6] believes that the key to success in treating patients with arthritis is given by a full consideration of all the etiologic factors involved. The etiologic factors are various, and in the great majority of cases, if not in all, there is more than one factor. In such cases, the more accurately the value of the particular factor is estimated and dealt with, the better will be the response to treatment.

The 500 cases were considered from the standpoint of focal infection, the possible and apparent foci being teeth, tonsils and prostate. On account of controversial opinion regarding the intestine as a focus, a consideration of it as such was omitted. Teeth were considered as possible foci only when dental roentgenograms, showing periapical rarefaction, had been made and recorded; tonsils only when close inspection had been made and pus had been expressed, or when the laryngologist had reported that the tonsil was definitely septic, and the prostate only after microscopic examination of the prostatic fluid. Some of the prostates investigated showed no evidence of infection on the first examination, but from three to five days later, following a provocative test, a large number of pus cells were found in the secretion.

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5. Ely, L. W.: The Second Great Type of Chronic Arthritis in Its Relation to Industrial Accident Cases, California and West. Med. **22**:260, 1924.

6. Horder, Thomas: Discussion on Treatment of Chronic Arthritis, Brit. M. J. **2**:633, 1925.

Ninety-four (58 per cent) of the women and 178 (52 per cent) of the men were referred for investigation of foci. Therefore, in discussing the incidence of focal infection, computation is necessarily limited to those cases receiving consideration from that standpoint. Of the sixty-two women who were referred for dental examination, fifty (80 per cent) showed periapical infection, and of the 125 men referred, ninety (72 per cent) showed similar involvement. Ten (15 per cent) of sixty-seven women and twenty-eight (20 per cent) of 138 men whose noses and throats were examined showed definite tonsillar sepsis. Other reports on the condition of the tonsils examined were given in thirty-nine of the women and in 111 of the men. Thirty-nine men were referred for prostatic investigation, of whom thirty (77 per cent) showed definite prostatic infection.

Besides the patients showing periapical involvement, there were nine women and twenty-eight men whose dental examination revealed pyorrhea without periapical infection. Therefore, if in addition to the patients with definite infection at the apexes, those showing pyorrhea alone are added, twenty-eight men and nine women, the proportion of dental infection is raised from 72 to 94 per cent in the men and from 80 to 95 per cent in the women. Eleven women and thirteen men had had all teeth extracted previously, presumably on account of infection, and, although they cannot be included in this computation since they were not referred for dental roentgenograms, they serve to increase the possible percentage of cases in which teeth may be considered as foci.

I have already mentioned other reports on the tonsillar conditions, of which thirty-nine were given in the cases of women and 111 in those of men. The determination of infectious potentialities of a tonsil by inspection is not always accurate, and doubtless many real foci are included in those cases not reported as definitely septic. C. H. Mayo [7] has often emphasized that it is not always the large red tonsil that is most to be feared; that the small shriveled one which has lost the power to react against and localize its infection and harbors it in a crypt, sealed away from the exterior, is a source of danger. Twenty-three men and nineteen women gave histories of recurring attacks of tonsillitis or of having undergone tonsillectomy previously. In a certain percentage of these cases it might also reasonably be assumed that the tonsils had been active foci. Therefore it becomes apparent that, although but 20 per cent of the men and 15 per cent of the women who underwent tonsillar examination gave definite evidences of septic tonsils, these percentages might well be considerably increased, speculatively at least, if this more or less indeterminate group were considered.

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7. Mayo, C. H., quoted by Hench, P. S.: The Systemic Nature of Chronic Infectious Arthritis, Atlantic M. J. **28**:425, 1925.

Von Lackum and Holloway,[8] of the Mayo Clinic, have reported several cases of primarily infectious arthritis of the spine, as well as some of this type under discussion, in which relief or amelioration of symptoms referable to the spinal condition was obtained through treatment of the inflamed prostate, so that now, in all cases of arthritis of the spine producing symptoms, it is customary to make a thorough examination of the prostate. Seventy and nine-tenths per cent of the patients of this series who had incidental spondylitis had some form of prostatic disease, as has been noted, including all forms encountered in the diagnoses. However, of the entire group of 340 men, the diagnosis of prostatitis was made in only forty-five cases (13.2 per cent). Intensive investigation of the prostate in thirty-nine revealed that thirty (77 per cent) had definite prostatic infection. I shall not venture even to intimate that this large incidence of pathologic conditions of the prostate may indicate that prostatic disease is an etiologic factor in the development of this type of arthritis, but it is a most interesting coincidence that the incidence of disease of the prostate in 360 cases was 70.9 per cent, and the occurrence of hypertrophic arthritis of the spine in more than 1,400 cases was 67 per cent. They are probably merely parallel manifestations of approaching age. In any other series of men over 50 a large proportion would be observed to have prostatic disease.

Under a discussion of possible etiology various forms of chronic trauma, including that associated with obesity, must be considered, and therefore an analysis was made of the frequency of occurrence of obesity. All patients who weighed more than 200 pounds (90 Kg.) were included in the obese group, also a few who weighed less, but were of short stature (table 7). The lightest patient weighed 160 pounds (72.6 Kg.), and was 5 feet 2 inches (157.5 cm.) tall. Only a small percentage of the patients were obese.

As mentioned before, certain forms of arthritis or osteo-arthritis seem to be essentially accompaniments of middle and late life and manifestations of approaching old age. According to Fisher,[9] in the hieroglyphic writings "the determination of old age was the figure of an old man crippled with arthritis." Therefore I made note of "other evidences of senescence" in the case histories analyzed (table 8). Under one group I have listed the evidences of senile retrogressive change apart from the hypertrophy of the prostate in order that the comparison between the sexes might be less disproportionate. The evidences consisted of those

8. Von Lackum, W. H., and Holloway, J. K.: Chronic Prostatitis with Special Reference to Its Focal Aspects, M. J. and Rec. **122**:23 and 64, 1925.

9. Fisher, A. G. T.: A Contribution to the Pathology and Etiology of Osteo-arthritis: with Observations Upon the Principles Underlying Its Surgical Treatment, Brit. J. Surg. **10**:52, 1922.

observations, encountered in the course of the average clinical examination, which betoken old age; palpable sclerosis of peripheral vessels, sclerosis of retinal arteries as seen with the ophthalmoscope, coronary sclerosis as suspected from the anamnesis, arcus senilis and the general appearance of the patient, such as one who was described as a "wizened up old man."

About one fourth to one third of the patients, therefore, showed other evidences of senescence. It is my belief that the condition "incidental hypertrophic arthritis" of the spine, as I have chosen to term it, is in no small degree a degenerative or senescent type, especially in men. Its presence in two thirds of 1,415 men more than 50 years of age would seem to support such a contention. Whether it is referred to as metabolic or traumatic or as due to the stress and strain of life is of little

TABLE 7.—*Incidence of Obesity among Five Hundred Patients with Hypertrophic Arthritis of the Spine*

	Total Cases	Obesity	
		Cases	Per Cent
Men	340	37	10.9
Women	160	31	19.4

TABLE 8.—*Evidences of Senescence Associated with Arthritis*

	Total Cases	Including Hyperprostate in Men		Excluding Hyperprostate in Men	
		Cases	Per Cent	Cases	Per Cent
Men	340	241	71.0	110	32.3
Women	160	39			24.3

moment, for fundamentally retrogressive metabolism and trauma are but different factors in the same process, and so these other evidences of senescence are interesting accompaniments. Fisher [10] noted arteriosclerosis in the vessels of the synovial membrane, but considered the change in the vessels as merely coincidental. He believes that arteriosclerosis is inflammatory in origin, and therefore attributes the same cause to hypertrophic arthritis. In the cases reported by Swett,[11] arteriosclerosis and hypertrophic arthritis coexisted, and he considered the etiology of both to be the same. Peripheral and coronary sclerosis, arcus senilis, gray hair, hypertrophy of the prostate or atrophy of the uterus and senile vaginitis, with senile tremors, the stooped posture and hypertrophic arthritis form a decisive clinical picture of the senescent person.

10. Fisher, A. G. T.: The Nature of the So-called Rheumatoid Arthritis and Osteo-arthritis, Brit. M. J. **2**:102, 1923.

11. Swett, P. P.: The Association of Arterial Hypertension and Chronic Arthritis, Am. J. Orthop. Surg. **15**:635, 1917.

Why the incidence of the arthritis should be 67 per cent in men and only 40 per cent in women I cannot explain. Nor can I give a reason for the frequency of Heberden's nodes in women and their rarity in men, or why so relatively few women have angina pectoris. Allbutt [12] says that hospital records show that the proportion of men to women with arteriosclerosis is 3 to 1. His experience in private practice, however, does not substantiate this; he believes that the difference between the sexes in this liability, "at any rate to the descrescent kind," is inconsiderable. If arteriosclerosis is greater in men it may be considered a factor or rather as an indication that phenomena of senescence are more apparent in men.

However, if it is possible that a focus of infection in the prostate in cases of hypertrophic arthritis has a particular affinity for the spine, in view of the great number of pathologic conditions of the prostate in this series, the difference in incidence might be thus partially explained. It is interesting to note in this connection that carcinoma of the prostate rarely metastasizes to regions other than the lumbosacral spine. But as the prostate was investigated as a possible focus in only thirty-nine of the 340 men, and as 77 per cent of this group showed definite infection, the relative importance of prostatitis as an etiologic factor in this series can be only surmised, not conclusively stated.

Furthermore, to such possible etiologic factors as trauma, men are much more vulnerable than women, due to their greater exposure. Henderson [13] has noted that hypertrophic arthritis of the spine is common in laboring men over 50. The counterpart of this is in the relative rarity of arthritis of the spine in women just referred to, while they have the marked preponderance of Heberden's nodes. The latter might be explained on the basis of mild chronic trauma incident to woman's "handiwork." Ely believes, though, that trauma is the cause of symptoms but not of the disease itself; that is, that it acts by spraining a joint already damaged by disease,

The practical application of the observations in this department concerns itself, therefore, with a rational therapeutic point of view and gives a basis for the development of certain principles of conservative treatment when considering the observation of such "incidental arthritis." If two thirds of the men past the age of 50 have demonstrable hypertrophic arthritis of the spine, and if of this large majority relatively few give symptoms definitely due to the disease process, the clinician's attitude on encountering such a case should be one of conservatism. To subject a patient of 60 to an extraction of teeth or tonsillectomy or other surgical intervention for focal infection solely on the basis of a positive

12. Allbutt, T. C.: Diseases of the Arteries, Including Angina Pectoris, London, The Macmillan Company, 1915, vol. 1, p. 534.

13. Henderson, M. S.: Personal communication.

roentgenogram of hypertrophic arthritis of the spine with only mild symptoms, is hardly advisable, to say the least. In other words, this may be considered in the nature of a basis for a more rational and conservative consideration of the senescent and arthritic patient. Severe and disabling symptoms or evidences of a definitely progressive type of arthritis would justify more radical procedures. Such cases are most infrequent, however, and in the vast majority of them reassurance only should be necessary.

A second practical consideration is the medicolegal aspect, especially in reference to cases resulting from industrial accidents, a point which Ely has emphasized. A man wrenches or twists his back while at work and complains of pain and then of disability. Roentgenograms show the characteristic lipping and spurring of hypertrophic arthritis, and when the case is called for adjudication the question at issue is whether the injury is responsible for the arthritic changes shown in the roentgenogram. To grant this would be to deny the rôle attributed to the factors here considered—infection and the metabolic and senescent phenomena. That trauma may play some part in the etiology of hypertrophic arthritis is true, but by the term trauma, as I have used it, is meant long-continued irritation of mild or moderate degree. To these factors is now added the fact that two thirds of the cases of this particular type of arthritis are found incidentally in patients undergoing investigation for complaints not germane to this particular condition. Therefore, the improbability of one single injury's being responsible for the observations of hypertrophic arthritis is obvious.

SUMMARY AND CONCLUSIONS

Apparently this "incidental" hypertrophic arthritis of the spine is the result of a combination of factors and not of any one factor. Infection plays a rôle, as indicated by the presence of foci in a fairly high percentage of cases. Chronic trauma is also a factor, particularly in the obese group, presumably with exposure to irritation. Senescent or retrogressive metabolic changes are important causes.

If there are no symptoms treatment is unnecessary. With moderate symptoms conservative treatment is indicated. This would include primarily the total procedures of baking and massage and graded exercise. The conservative consideration of the removal of foci is then justified. Whenever possible, the element of trauma should be minimized, especially in the obese group, by reducing the weight or by other means.

In a series of 2,090 patients more than 50 years of age, for whom roentgenograms of the kidneys, ureters and bladder were taken during 1925, 40 per cent of the women and 67 per cent of the men showed hypertrophic arthritis of the spine, which condition I have designated as "incidental hypertrophic arthritis of the spine."

The case histories of 160 women and 340 men of the group with arthritis were analyzed in detail. On account of the nature of the group chosen, the predominating type of chief complaint was genito-urinary, as were also the primary diagnoses. Of the men, 70.9 per cent showed diseased prostates. Seventy-four per cent of the men and 61.3 per cent of the women were without any complaint whatsoever of the various types of "rheumatic," neuromuscular and arthritic pains.

Of the women whose teeth were investigated as possible foci, 80 per cent had periapical infection; including those with pyorrhea, 95 per cent had dental sepsis. Of the men, 72 per cent had periapical infection; including those with pyorrhea, 94 per cent had dental sepsis. Of those undergoing thorough examination of the tonsils, 15 per cent of the women and 20 per cent of the men showed definite tonsillar sepsis; 75 per cent of thirty-nine men referred for examination of the prostate had definite infection.

The traumatic factor in the etiology is partially illustrated by the presence of obesity, in which the assumption of chronic trauma can be made in 24 per cent of the men and in 33 per cent of the women.

The degenerative or senescent nature of this "incidental" arthritis is shown by other evidences of senescence in 71 per cent of the men, including hypertrophy of the prostate, and in 32.3 per cent excluding this condition. Such evidences were present in 32.3 per cent of the women.

In view of the high incidence in persons beyond the age of 50, especially in men, of hypertrophic arthritis of the spine, which is without symptoms in a majority of patients, a plea is made for conservative consideration, advice and treatment in such cases.

The improbability that a single accident or injury is responsible for the development of hypertrophic arthritis of the spine is obvious.

A REVIEW OF UROLOGIC SURGERY

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KIDNEY

Experimental Surgery.—Perlmann and Kairis [1] report on resection of the kidney and transplantation of hemostatic tissue. Berti, in 1921, collected ninety-five cases of resection of the kidney; seventy-four patients were cured, seven were not cured, seven died, and in seven cases secondary nephrectomy was performed. Tuffier was the first to show, by animal experimentation, how small a portion of renal substance is necessary to support life. For animals, 1.5 Gm. for each kilogram of body weight is sufficient; for man, from 80 to 150 Gm. is necessary (Kümmell).

Four groups of experiments were performed. In the first group, from one fourth to one third of one kidney was resected, and the parenchymal wound packed with muscle or fat tissue. From six to twenty-seven days later, the opposite kidney was removed. Later the dogs were killed, and the resected kidney examined. In the second group, nephrectomy was performed first and resection at the second operation. In the third group, both kidneys were resected at the same time. In the fourth group, one kidney was removed and the opposite kidney was partially resected simultaneously.

One dog in group 3, in which the upper third of each kidney had been simultaneously resected, died from uremia three days after operation. Both the dogs in group 4, in which partial resection and nephrectomy were simultaneously performed, died, one ten days after operation from renal insufficiency, the second twenty-four hours after operation.

The other animals, in which the operations on the two kidneys were performed at different times, from one to three weeks apart, remained alive until killed for an examination of the site of renal resection.

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1. Perlmann, S., and Kairis, Z.: Ueber Nierenresektion, Ztschr. f. Urol. **20**:595, 1926.

Bayle [2] carried out a study on compensatory renal hypertrophy in rabbits after unilateral nephrectomy. The remaining kidney was examined at varying periods. Comparative studies of the two kidneys were made in regard to volume, weight, dimension and histologic structure. In twenty-six of twenty-eight rabbits the remaining kidney was greater in weight and volume than the kidney first removed. The increase in weight and volume reached its maximum and terminated at about the forty-fifth day. In no case did the remaining kidney equal twice the weight of the other kidney; however, it usually increased from 60 to 70 per cent. There is not an exact parallelism between the hypertrophy and the increase in renal function; the augmented function is attained rapidly, the hypertrophy slowly.

The compensatory hypertrophy is produced by an increase in the volume of the elements already present in the kidney, not by the formation of new tubules and glomeruli. The width of the renal cortex of the hypertrophied kidney is double that of the other, and the surface of the hypertrophied glomeruli is correspondingly augmented. The diameter of the tubules is also somewhat larger than the diameter of the tubules of healthy kidneys. Bayle concludes that in healthy animals the combined phenomena of hypertrophy and cellular hyperplasia in the remaining kidney compensate exactly for the loss of renal secreting tissue due to unilateral nephrectomy.

Carson and Goldstein,[3] in a study of experimental nephrotomy in dogs with only one kidney, found that dogs killed within forty days after nephrotomy showed no definite change in the size of the organ. However, in those killed after forty days, it showed some decrease in size after nephrotomy. Microscopic changes in the single kidneys were similar to those in dogs with the other kidney normal. In order to encourage destruction of the kidney, sutures were not used after nephrotomy.

Magoun studied the functional results of nephrotomy when sutures were employed, and was able to demonstrate a definite relationship between renal cell destruction and renal function; in other words, when much renal tissue was destroyed, renal function was reduced accordingly. Since microscopic study in Carson and Goldstein's series revealed a minimal destruction of renal tissue, even when only a single kidney remained, one can conclude that the function should be reduced only slightly.

These authors concluded that single or multiple nephrotomies without suture in dogs with a single kidney is a safe procedure, that

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2. Bayle, Henri: L'hypertrophie compensatrice du rein, Paris méd. **32**:121, 1926.

3. Carson, W. J., and Goldstein, A. E.: Experimental Nephrotomies: III. Nephrotomy without Sutures, in Dogs with Single Kidneys, J. Urol. **15**:505, 1926.

nephrolithotomy without suture in dogs is successful, and that histologic studies of nephrotomized kidneys without suture demonstrate a minimal destruction of renal tissue.

Andler [4] states that the frequent occurrence of accessory renal vessels is due to the persistence of embryologic structures. Accessory vessels to the lower pole may cause stasis in the renal pelvis. The presence of these vessels and hydronephrosis does not always imply a simple relationship. In a strict sense they are not the cause of hydronephrosis, the vessels becoming causative agents only under certain conditions. The renal pelvis or the upper ureter can come in contact with accessory vessels, either by dislocation of the kidney or dilatation of the renal pelvis and ureter. With marked dilatation of the renal pelvis, a valve is formed at the ureteropelvic juncture, which may cause definite obstruction. Pyelographic and functional studies of the kidney are indispensable for a diagnosis which should be determined as early as possible.

The best treatment is early nephropexy with severance of the accessory vessels. The latter will not have unfavorable consequences. If a valve formation is present, it should be remedied by a plastic operation if possible, otherwise nephrectomy should be performed. Conservative surgical intervention is indicated for bilateral conditions or when the opposite kidney is subject to some disease. Infected hydronephrosis is a contraindication for conservative surgical intervention when the condition is unilateral.

[Ed. Note.—The severance of accessory renal vessels is not always accomplished without harm to the kidney. The experimental work of Belt and Joelson [5] clearly showed that severance of a renal arterial branch causes necrosis of the area supplied by that vessel with, as an end-result, a depressed stellate scar equal in area to the region supplied by the ligated branch. The magnitude of such an area depends directly on the size of the ligated vessel. While this necrosis may not be extensive enough to produce clinical evidence of renal insufficiency, it definitely decreases the amount of renal reserve tissue, for restoration of function in such areas is revealed through their work to be anatomically impossible. When vessels of large size bridle the ureter and cause hydronephrosis, Quinby [6] has advocated free division of the ureter followed by its reimplantation into the most advantageous position of the pelvis away from the vessel. It must be remembered that anomalous conditions are frequently bilateral, and hence there remains a potential source of similar

4. Andler, Rudolph: Neuere Erfahrungen über die pathologische Bedeutung akzessorischer Nierengefässe, Ztschr. f. urol. Chir. **19**:305, 1926.

5. Belt, A. E., and Joelson, J. J.: The Effect of Ligation of Branches of the Renal Artery, Arch. Surg. **10**:117 (Jan.) 1925.

6. Quinby, W. C.: Hydronephrosis, Tr. Am. A. Genito-Urin. Surg. **15**:43, 1922.

trouble on the opposite side, even in those cases in which it has as yet given no clinical evidence of its presence. On this account the procedure of choice is one which will result in the least destruction of renal tissue.]

Surgical Treatment in Nephritis.—Damski [7] publishes his personal experience with cases of nephritis of different types in which surgical intervention was necessary, to which he adds 110 cases of other authors. He draws the following conclusions. In cases of unilateral hematogenous nephritis, the diseased kidney should be exposed and radically operated on according to the degree of its destruction, even nephrectomy being performed at times. In ascending nephritis, the treatment should be expectant, except in serious cases with marked retention or infection, in which surgical measures are necessary; nephrectomy is contraindicated by the possible bilaterality of the lesions. In hemorrhagic, painful nephritis, in which category most of the cases of essential hematuria should be placed, operation is indicated; the most satisfactory operation is decapsulation, with nephropexy in cases of nephroptosis. Theoretically, in toxic nephrosis, especially that produced by sublimate, decapsulation should be performed, but in fact it does not produce a favorable result, as the toxic process involves not only both kidneys, but also the digestive tract. Damski agrees with most other authors in saying that in cases of chronic interstitial nephritis, mainly acute or subacute nephritis with oliguria, or anuria with edema, or serious uremia, the treatment should be decapsulation; cure has never been observed, but the amelioration may be of long duration. It is not in our power to influence the sclerotic or cirrhotic processes of glomerulonephritis, with or without signs of nephrosis. One of the author's cases proves also that decapsulation is of no value, and even harmful, in cases of advanced chronic nephritis with cirrhosis and arterial hypertension.

Hydronephrosis.—Caulk [8] states that the trend of modern renal surgery is toward conservatism, and that as a result many kidneys that would have been removed have been left to function. He reports a case of resection of a stricture of the superior renal pelvis for the relief of partial hydronephrosis. At operation it was noticed that entrance from the true pelvis to the upper superior part was markedly constricted. Partial nephrotomy was performed over this region in the upper part of the kidney, the renal substance being opened down into its pelvis. The upper part was moderately dilated, but still retained healthy cortical substance. It was impossible to enter the upper pelvis from below because of a dense scar. This mass of scar tissue was exposed and resected until the pelvis from below would admit one finger. A rubber

7. Damski, A.: Sur le traitement chirurgical des nephrites, J. d'urol. **21**:203, 1926.

8. Caulk, J. R.: Resection of Stricture of the Superior Renal Pelvis for Relief of Partial Hydronephrosis, Surg. Gynec. Obst. **43**:279, 1926.

tube was inserted through the incision which had been made through the renal tissue, through the renal pelvis, and the resected area down to the true pelvis. Recovery was uneventful, and pyelograms show that the renal pelvis fills and that there is no retention in it.

Anomalies.—Boss [9] enumerates the factors in the diagnostic determination of the presence of horseshoe kidney. Frequently the condition is associated with defects of the general constitution, such as psychic impairment, physical developmental anomalies in other organs or a "hypoplastic lymphatic development."

Symptoms due to the pressure of the fused kidney on other organs, or pain from pressure of a broad isthmus on the vertebral column or aorta are sometimes suggestive in the diagnosis. Inspection and percussion as a rule give little positive information. Occasionally tumor and, rarely, stone may be felt in one half of a horseshoe kidney. The Schreiber-Seelig palpation albuminuria test may be of value.

In themselves cystoscopy and chromocystoscopy are of little diagnostic worth, but the introduction of opaque catheters and subsequent roentgenography with pyelo-ureterography are of the greatest importance. When the catheters stop at a relatively low level on each side, horseshoe kidney is to be considered a possibility.

The direct roentgenogram is of value, according to Voorhoeve, in that it may demonstrate the following features: a vertical position of both kidneys, the inner edge running parallel to the vertebral column; a median displacement of both kidneys (the distance between the median edge of the kidney and the vertebral column is abnormally small); bilateral ptosis of the kidneys; immobility of the kidneys in a mediolateral direction, while mobility in an axial direction can be determined; apparent displacement of the lower renal pole in relation to the spinal column, and visibility of the connecting isthmus. Seldom are all of these roentgenographic features present. The abnormal roentgenographic relation of the colon to the low and medial horseshoe kidney in contrast to its position with reference to the ribs and spinal column may be of diagnostic significance, especially if the stone has a long axis which is not in the direction of the usual ureteral course.

By far the best and most positive information is revealed by pyelo-ureterography. Usually the renal poles are displaced so that the lower lies nearer to the vertebral column than the upper; the poles of the two kidneys tend to converge, usually below. Again the insertion of the ureter is usually placed at an anomalous point, often below and lateral to the pelvis. Bilateral pyelography frequently demonstrates the relation of one kidney to the other in such a way that the connecting bridge is better localized for operative attack.

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9. Boss, William: Zur Diagnose der Hufeisenniere, Ztschr. f. urol. Chir. **19**:15, 1926.

Certain features noted at operation are worthy of mention: the peritoneal fold extends far laterally; the fatty capsule of the kidney is poorly developed; the renal fossa is shallow; the suprarenals are not superimposed on the upper pole; there is marked lobulation of the renal surface, and many adherent vessels are encountered. The site of the pelvis is usually on the anterior face of the kidney, thus making its approach for pyelotomy somewhat easier. The ureter may be flattened out over the isthmus. In case the kidney is to be saved after division of the isthmus, care should be taken that the ureter is freed and its proper course maintained by nephropexy.

[Ed. Note.—The diagnostic features mentioned, aside from pyelography, are for the most part indeterminate and hardly to be relied on. Since the advent of urographic study in its various details much has been learned with regard to horseshoe kidney. Before this time the diagnosis usually was made at the operating table. With careful pyelograms, however, at the present day it is possible in most instances to establish the diagnosis and to determine the operative procedure to be followed.]

Schillings [10] reports a case of heminephrectomy for pyonephrosis in a horseshoe kidney. He reviewed the reports of 108 cases of surgically treated horseshoe kidney. In only twenty-two was the diagnosis made before operation. In twenty cases there was no lesion; eighteen showed hydronephrosis; eleven, pyonephrosis; twelve, tuberculosis; thirty-two, stones; four, neoplasms, and three, cysts. There were two cases of nephritis and two of trauma to the kidney; one case was complicated with a fistula and one with a ureteral stone. Heminephrectomy was performed in fifty-two cases; eight patients died. Palliative operations were performed in thirty-seven cases, with death in four.

Haas [11] comments on the relative frequency of horseshoe kidney, more than 300 cases having been described. Usually, through the obstruction to the urinary outflow, the conditions for the development of hydronephrosis, pyonephrosis and calculus are present. The usually demonstrable abnormal course of the ureter over the inferior renal pole with its consequent compression is noteworthy in this connection.

Tumors in horseshoe kidney are rare. The few cases published are remarkable, as all but one (a cystic tumor in the isthmus) have occurred in the right division of the double kidney. Haas describes an unusual case in which the resected right side of a double kidney showed three different types of renal tumor. The patient was a woman, aged 45, who had suffered from hematuria, pain in the right side and fever at intervals for three and a half years. Shortly before she was admitted

10. Schillings: Le rein en fer à cheval, abstr., Ztschr. f. urol. Chir. **19**:410, 1926.

11. Haas, N. C.: Tumoren in Hufeisennieren, Ztschr. f. Urol. **19**:81, 1925.

to the hospital, a papilloma of the bladder had been removed by fulguration. Because of persistence of pain and a mass in the right side about the size of a child's head, the patient was admitted to the hospital. On cystoscopy a gaping right ureter from which blood came in a thick stream was noted. The left ureter revealed clear urine, and the function of the left side was normal. At operation the right kidney was found to belong to the horseshoe type and was resected at the isthmus. In the specimen removed a hypernephroma the size of a fist was found in the upper pole, an adenoma the size of an egg in the lower third and a small papilloma in the lower division of the pelvis. The pathologic differences between the tumors were verified microscopically.

[ED. NOTE.—The occurrence of several types of tumor in the same organ is rare, but is occasionally seen. When a large mass is noted in the region of the kidney associated with papilloma of the bladder, the possibility of papilloma of the renal pelvis being present must be borne in mind. The case described, in which three separate neoplastic entities were encountered in the same kidney, belongs in the realm of pathologic curiosities.]

Siedner [12] reports a case in a woman, aged 32, who complained of renal colic on the left side. There was diminished function in the left kidney. The pyelogram showed a second cup-shaped pelvis above the normal pelvis, with its own ureter which joined the ureter of the normal pelvis at an acute angle. At operation this ureter was transplanted to the pelvis of the normal kidney, since its opening appeared stenosed. Convalescence was uneventful, and the patient was free from pain three months later, at which time the renal function had increased.

Anomalies and Calculi.—Harbitz [13] notes that Motzfeldt, in 1914, collected an enormous amount of material dealing with anomalies of the kidneys and ureters. Motzfeldt studied the reports of about 4,500 necropsies. Harbitz carried on a similar series of investigations, studying 942 necropsies of infants and 2,336 others. From these two series of necropsies, 7,778 in all, the following features were determined.

There were 161 instances of renal or ureteral anomalies (about 2 per cent), twenty-two cases of renal aplasia, twenty-two of renal hypoplasia, eighteen of horseshoe kidney, nine of ectopic kidney, thirty-seven of double ureter, forty-eight of kinks or congenital valve formation in the ureters with congenital hydronephrosis and five of cystic kidney. The number of anomalies reported is too small, as single cases of ureteral abnormality may easily escape attention. In the opinion of Harbitz, the number should probably run about 3 per cent higher.

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12. Siedner: Zur Operation von Doppelnieren, Ztschr. f. Urol. **19**:842, 1925.

13. Harbitz, F.: Ureterabnormitäten: Nephrolithiasis, Norsk Mag. f. Laegevidensk. **86**:94, 97, 105 and 113, 1925; abstr., Ztschr. f. urol. Chir. **19**:70, 1926.

Concerning the general conditions predisposing to the formation of calculus, Harbitz feels that a metabolic diathesis plays a great rôle in the formation of urate and oxalate stones, while infection is the important factor in the formation of phosphate stones. In necropsy material urate stones were more commonly found, in contrast to what is seen in surgical cases. The oxalate stones are relatively small, have sharp edges and for that reason may be associated with hemorrhage more frequently than the others. Calcium carbonate stones occur infrequently. They are white and hard. Among the rarer stones Harbitz mentions, besides cystin calculi, one of indigo in a 7 year old child who had had indigo in the urine for a rather long time and had died of intestinal tuberculosis.

[ED. NOTE.—This is an unusually large series of cases from necropsy material, and is of some value from the standpoint of geographic pathology in that it comes from a Norwegian source. The frequency with which renal and ureteral anomalies occur varies in detail with every long list of pathologic specimens studied, but on the whole Harbitz' review corresponds fairly well to that of European and American writers. As regards the structure of stones, there is a great divergence of statistical opinion with every series of stones analyzed. Likewise the question as to whether urate and oxalate calculi are the product of increased excretion of their chemical constituents (a so-called metabolic diathesis) or are due to renal infection is debated, and, in spite of much experimental work during the last six years, must be considered unsettled.]

Nephrolithiasis.—Kairis [14] states that nephrolithiasis may be diagnosed either by colic, renal bleeding and passage of stone or by roentgen-ray examination. In modern diagnosis the latter is sufficient. There has, however, been a certain percentage of cases of failure of the roentgen ray to cast a shadow; in European clinics this figure is from 3 to 5 per cent. American observers have placed it at from 10 to 15 per cent. Many of these stones have been made visible by pyelography.

Kairis reports a case in a woman, aged 37, with pain in the region of the left kidney. A plain roentgenogram was negative. Pyelography revealed a stone in the left renal pelvis. Six months later, the plain roentgenogram gave a positive picture of the stone. Pyelotomy was performed. The stone was found to be composed of calcium oxalate and calcium phosphate. Kairis believes that the lack of cementing substances was the cause of its failure to cast a shadow at an earlier date.

Marion [15] demonstrates the advantage of ureteral catheterization in ureteral colic due to calculi. He states that the patient is usually

14. Kairis, Z.: Beitrag zur Klinik und Diagnostik der Strahlendurchlässigen Nierensteine, Ztschr. f. urol. Chir. **20**:66, 1926.

15. Marion, G.: De l'utilité du catheterisme urétéral dans la colique nephrétique par lithiase, Presse méd. **33**:1043, 1925.

relieved as soon as a catheter passes the stone, and the pelvis empties. Marion is an ardent advocate of leaving the ureteral catheter in place, even for several days, but does not advise it in every case. He limits it usually to cases in which there is repeated colic, without passage of the stone and accompanied by fever. In one of his cases a woman had attacks of severe right renal colic for three years. The last crisis was of three weeks' duration, but not accompanied by fever; it could be controlled only with morphine. The ureter was easily catheterized, and the pain was immediately relieved. The roentgenogram showed a stone the size of a cherry in the upper ureter. In a second case there was pain in the right ureteral region of twenty-five days' duration. The diagnosis lay between renal and gallbladder colic. Ureteral catheterization was carried out; an obstruction, which was overcome, was encountered 17 cm. above the ureteral orifice. The pains ceased completely after several hours. The catheter was left in place for twenty-four hours. Oil injections were given. The roentgenogram showed a stone in the upper third of the ureter. Eight days later the stone was passed spontaneously. In a third case, chills, vomiting and other serious symptoms accompanied the colic. Ureteral catheterization revealed an obstruction 15 cm. up; a small ureteral bougie was passed. There was moderate fever for ten days, after which a new attack of pain set in. Ureteral catheterization was again performed, and as the catheter was engaging the ureter, the stone fell into the bladder. Marion also believes in the use of belladonna in preference to morphine.

Renal Tuberculosis.—Rovsing and Frode [16] reviewed their cases of renal tuberculosis: 632 cases from 31 various hospitals; 78 of these cases were eliminated. Analyzing the remaining 554 cases, they come to the following conclusions. Urinary tuberculosis occurs most frequently between the ages of 20 and 40, a little earlier in women than in men. The right kidney is more commonly affected, especially in men. Renal tuberculosis at times shows itself macroscopically as a diffuse process; when there is but one focus, it is usually in the upper pole. In 85 per cent of cases there were macroscopic changes in the ureter. Trauma and gonorrhea have no relationship to the occurrence of urogenital tuberculosis. In women it frequently occurs in association with pregnancy. The initial symptom of renal tuberculosis is usually dysuria (62 per cent), less frequently renal pain (25 per cent) and occasionally hematuria. However, in the course of the entire disease, hematuria occurs in 50 per cent of cases. Albuminuria is present in 11 per cent, while pyuria is practically always present. Bacilli of tuberculosis were found

16. Rovsing, Thorkild, and Frode, Rydgaard: Klinische Untersuchungen über die Tuberkulose der Harnwege, Bibliot. f. Laeger **117**:225, 1925; abstr., Ztschr. f. urol. Chir. **19**:415, 1926.

in 78 per cent of cases. After nephrectomy, 13 per cent of the patients died while in the hospital; 9.8 per cent of the patients died from tuberculosis, general or affecting the remaining kidney, 3.2 per cent of them from operative complications. Technically it was found important in nephrectomy that the ureter be entirely removed through a buttonhole incision in the iliac fossa. Records showed that 62 per cent were well following nephrectomy. Death usually occurred within the first year after nephrectomy and was generally due to tuberculosis of the remaining kidney or other organs. Postoperative treatment is important, especially in lesions of the bladder, which were treated with irrigations of phenol solution if they did not heal spontaneously.

Hofmann [17] describes a case in which the bladder showed tuberculous changes, and, by inoculation of animals, tuberculosis of the right kidney was demonstrated. The patient refused operation, went to Kissingen and was treated with sun baths, rest, artificial sunlight and injections of tuberculin. About a year later he came under observation on account of tuberculosis of the left epididymis. The urine, however, was completely clear, and cystoscopy revealed a normal bladder with none of the tuberculous changes previously seen in the wall of the bladder or at the right ureteral orifice. Ureteral catheters returned clear urine from both sides, which was negative on inoculation of animals. Orchidectomy and epididymectomy on the left side revealed the typical picture of tuberculosis in the parts removed.

Hofmann feels that the case mentioned shows the possibility of renal tuberculosis being cured by conservative medical treatment, at least in rare instances.

[ED. NOTE.—Such reports as that of Hofmann appear from time to time in the literature and are of more than passing interest in that urologists of the present day generally hold that spontaneous cure of renal tuberculosis does not occur, and that relief is to be sought only when surgical measures are applicable. The contention might be raised that in Hofmann's case the kidney which he considered sound is still tuberculous, the process having been walled off (corresponding to the closed parenchymatous or occluded type described by Halle, Zuckerkandl and Braasch) in such a way as to prevent the escape of bacilli or pus cells into the urinary stream.]

Falci [18] states that renal tuberculosis is a more serious disease in children than in adults. Fifty cases of renal tuberculosis were observed in children. Fourteen cases became bilateral, twenty-five remained unilateral and eleven disappeared from observation. Four patients were

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17. Hofmann, Willy: Ueber ein Fall von konservativ geheilter Nierentuberkulose, Zentralbl. f. Chir. **52**:1025, 1925.

18. Falci, Emilio: La tuberculose rénale de l'enfant (frequence, evolution, pronostic) comparée à celle de l'adulte, J. d'urol. **20**:300, 1925.

between 1 and 6 years of age, eight between 7 and 12 years, and forty between 13 and 18 years. There were twenty-six boys and twenty-four girls. In thirty-six cases (72 per cent) the lesion was unilateral and in fourteen (27 per cent) bilateral. In a series of 177 adults, it was unilateral in 152 (85.8 per cent) and bilateral in twenty-five (14 per cent). From this it is seen that in children the disease is more frequently bilateral. Further analysis shows that with increase in age in children, the tendency toward bilateral disease decreases. In adults this also occurs up to the age of 50, after which there is a tendency toward marked diminution in the percentage of bilateral lesions. Five children with bilateral disease lived from one month to four years. Three of eight more cases were lost sight of and five are living, but are in poor health. Of twenty-five patients operated on, eleven (44 per cent) died; in four the condition became worse and in four it remained stationary; six (24 per cent) were cured. Death was usually caused by generalized tuberculosis. In adults the number of cures is equivalent to 50 per cent as against 24 per cent in children.

Pazzi [19] notes the association of calcified retroperitoneal and mesenteric lymph nodes in cases of renal tuberculosis. Occasionally these may be confused with renal and ureteral calculi by their form, position and radiologic relationship. In one case of renal tuberculosis a small round shadow was found in the corresponding renal field. This was thought to be caused by calcified lymph nodes. Studies with the roentgen-ray catheter and pyelography did not clear the situation; in fact, two additional shadows were found in the region of the lower pole. On examination the removed kidney showed that these shadows were caused by areas of caseation in the kidney. In another case of renal tuberculosis in a man aged 45, there was a shadow in association with the kidney. It was impossible to determine whether this was a stone or a lymph node. All studies on the kidney gave negative results, except to reveal tuberculosis of the corresponding kidney. Following nephrectomy, roentgenograms still showed the same shadow. In a third case with a specific history, all urologic studies for tuberculosis were negative. Nevertheless, roentgenograms showed two small round shadows in the region of the left ureter. Further studies showed that these shadows lay outside of the ureter.

Hels [20] has gathered his material from 377 cases of nephrectomy for renal tuberculosis in which there were definite records concerning the treatment of the ureter and the course of healing of the wound.

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19. Pazzi, Ermanno: Gangli calcificati nella tuberculosi renale, Radiol. med. **12**:536, 1925; abstr., Ztschr. f. urol. Chir. **19**:415, 1926.

20. Hels, Robert: Ueber die Technik der Nephrektomie wegen Nierentuberkulose mit besonderer Berücksichtigung der Behandlung des Ureters, Bibliot. f. Laeger **117**:258, 1925; abstr., Ztschr. f. urol. Chir. **19**:418, 1926.

In forty-two cases the ureter was resected through an incision in the iliac fossa with healing by primary union in 78.5 per cent, ureteral fistula in 9.5 per cent and tuberculosis of the soft tissues in 2.5 per cent; in 219 cases in which the ureter was removed through the nephrectomy incision, healing by primary union occurred in 74 per cent, ureteral fistula in 5 per cent and tuberculosis of the soft tissues in 17 per cent; in 116 cases the ureter was buried, with primary union in only 49 per cent.

[ED. NOTE.—Thevenot states that primary ureterectomy for renal tuberculosis has been abandoned in France, since in many cases it is useless, or it aggravates the postoperative condition. Persson states that the best results are obtained by simple primary suture after nephrectomy. In sixty-two of sixty-four cases in which the ureter was ligated and dropped into the wound and primary suture carried out, the wound healed in two weeks. Whenever any infection occurred, the wound was usually drained for three or four days only.]

Walters of the Mayo Clinic reported on the disposal of the ureter in 282 cases of nephrectomy for tuberculosis; in all cases complete data were obtainable. Ligation of the ureter with catgut and sterilization of the cut end with the cautery seems to have been the most effective means of treating the tuberculous ureters in which there was not sufficient stricture to produce distention. In 48 per cent of these cases there was primary union of the incision before the patient was dismissed from observation. The incisions remained healed without subsequent drainage. Twenty-seven per cent of patients similarly treated, whose incisions were draining when they were dismissed (from three to five weeks after operation), report subsequent permanent healing of their wounds.

Another method used in the Mayo Clinic was suturing the cut end of the ureter to the margin of the skin at the lower angle of the incision. This allowed escape of the contents of the ureters to the outside without contamination of the wound. This method has now been practically discarded in the Clinic, and it is interesting to note by actual comparison of the various methods, used for a period of seven years, that this one is ineffective, as measured by primary healing of the wound. Walters states that the results of partial or complete ureterectomy with nephrectomy, as measured by healing of the wound and ultimate end-results in fourteen cases of stricture of the tuberculous ureter insufficient to produce obstruction and distention, do not warrant the employment of the procedure as a routine. The cases of demonstrable stricture and distention of tuberculous ureters obviously form a separate group, since the stricture forms a closed sac if it is distal to the cut end of the ureter. W. J. Mayo now removes all ureters with the kidney if the constricted ureter is distended to a point below the stricture. In the other cases he

clamps the ureter with a hemostat without separating it from its fatty sheath, in order not to disturb its circumureteral circulation, divides it with the cautery and drops it back without a ligature, which he believes might act as a foreign body. After thorough hemostasis the incision is closed without drainage. After his study Walters concludes that, following nephrectomy for primary renal tuberculosis, the method of compression of the stem of the ureter, ligation with catgut and sterilization of the cut end by the cautery produces the best end-results as measured by primary healing of the wound. Improvement takes place in vesical symptoms and in general health independent of drainage of the wound in the ureter after nephrectomy.

Young [21] states that uncomplicated cases of renal tuberculosis are rare; the bladder is involved in about 40 per cent and the genital tract in about 26 per cent of cases. Genito-urinary tuberculosis is only rarely seen in large tuberculosis sanatoriums; it was found in only sixty-five of 10,000 sanatorium cases. Genito-urinary involvement makes tuberculosis of the lungs infinitely more dangerous than when other regions are affected, such as the bones.

Young reviews 222 cases of tuberculosis of the genital tract. Of these the genital cases with renal involvement numbered 114; genital cases with doubtful renal involvement, eight; genital cases without such involvement, 100. Of the 222 cases in which the genital tract was affected, the kidneys were free in only 100, showing again the marked interrelationship in the disease. The epididymis was involved in 175, the seminal vesicles in 185. The epididymis was affected alone in thirty-seven cases, whereas the seminal vesicles were affected alone in forty-seven, showing that epididymal tuberculosis alone is the rarest of all forms of genito-urinary tuberculosis. In 191 cases of tuberculous infection of the prostate gland, the kidney was involved in eighty-six; in 171 there was other genital involvement.

Young states that nephrectomy can almost always be performed through a curved low incision, extraperitoneally. When the ureter is exposed, he thinks it is important to inject pure phenol into it to destroy, as far as possible, the tuberculous process in the mucous membrane. He does not think it wise to try to remove the entire ureter. The whole ureter cannot possibly be removed, and it is dangerous to have that last inch of the tuberculous ureter, opening into a deep, fresh, poorly-draining wound, instead of being brought near to the surface as a fibrous tube. He almost never removes the ureter unless it is large and distended. He injects phenol, ligates the ureter doubly and then excises the kidney.

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21. Young, H. H.: Tuberculosis of the Kidney, Its Diagnosis and Treatment, J. Michigan M. S. **25**:171, 1926.

Unilateral epididymectomy was performed in thirty-eight cases in which there was no involvement of the urinary tract; in twenty-six of these cases, the opposite epididymis had become affected and in six cases, the kidney. Only five of the thirty-eight patients are classed as well after five years.

The following table gives the results in cases of nephrectomy for tuberculosis.

Results of Nephrectomy for Tuberculosis

Total cases	112	
Well	53	(47.5 per cent)
Improved	24	(21.0 per cent)
Unimproved, vesical symptoms still present	18	(16.0 per cent)
Unimproved, recurrence in opposite kidney	4	(3.5 per cent)
Unimproved, recurrence in the epididymis	4	(3.5 per cent)
Total unimproved	26	(23.0 per cent)
Dead from tuberculosis since leaving hospital	8	(7.0 per cent)
Dead, operative	1	(0.89 per cent)
Total dead	9	(8.0 per cent)

In conclusion, Young states that tuberculosis of the urinary tract is complex, that involvement of both urinary and seminal tracts is common, that it is not sufficient to remove one focus of infection, but, if possible, the treatment of the kidney, seminal vesicles and epididymis should be radical and early, and that by radical operation excellent results can be obtained.

Munck [22] found that among 554 collected cases of urinary tuberculosis, fourteen were complicated with renal stone. In four cases the stone was apparently an etiologic factor in the origin of the tuberculous process in the kidney. In another case tuberculosis was found in one kidney and an aseptic stone in the other. In four cases following nephrectomy for tuberculosis, stones were found in the remaining kidney because of infection. In the remaining six cases it could not be determined whether the stone or tuberculosis was primary.

Tumors of the Kidney.—Legueu states that there has been no advancement in the last thirty years in the treatment of renal cancer. Radium therapy is of no value.

There is no way of determining the extent of the malignancy prior to operation. If the growth is larger than a hazelnut, the renal vein is usually involved, and in advanced cases it may even extend through the renal vein to the vena cava. If the tumor develops in the renal pelvis, it usually spreads into the ureter, the renal vein being more rarely involved.

Legueu [23] thinks that extension into the fatty capsule complicates the condition greatly and is often the cause of recurrence. In a series of

22. Munck, Jorgen: Nierentuberkulose und Nierenstein, Bibliot. f. Laeger **117**:245, 1925; abstr., Ztschr. f. urol. Chir. **19**:419, 1926.

23. Legueu: Les cancers du rein, J. d. Practiciens **39**:595, 1925.

thirty-seven cases the suprarenals were involved in eighteen. There is always in these cases a possibility of metastasis by way of the blood stream. The lymphatics along the renal vein and vena cava are occasionally involved and must be considered. In conclusion, Legueu states that in fair-sized growths, one can safely assume an involvement of the veins and the fatty capsule.

Dresser [24] states that comparatively little has been written about metastasis of hypernephroma to bone. The transmission is usually by way of the blood stream. In the fatty marrow, the blood channels are well formed, but the red marrow consists essentially of innumerable blood channels with extremely thin walls. The widening of the bed of the stream at its entrance with the red marrow must involve a considerable decrease in the rate of blood flow. Here conditions are ideal for the deposition of malignant cells floating in the blood stream. Thus it should be expected that the location of blood-borne malignant cells would conform to the anatomic distribution of the red marrow; and this is what occurs in most instances.

The diagnosis of metastatic lesions in bone is not easy; several points must be considered. The tumor may be vascular, giving a definite expansile pulsation, and when situated on the sternum may be confused with aneurysm. This may be ruled out by the demonstration of a normal aorta. The lesions are nearly always destructive, quickly eroding the bone and involving the soft tissues. No new bone formation may be seen, although spontaneous fracture through a metastatic nodule may complicate the picture of a purely destructive lesion by reason of the new bone formed in the process of repair.

Metastatic tumors are usually multiple, although occasionally single. Any bone may be involved, but metastasis distal to the humerus or femur is rare. The disease can occur at any age, and any point showing a destructive bone lesion should always be investigated for hypernephroma.

Prognosis is poor, although some patients have lived five years or more without treatment. Palliative results may be expected from high voltage roentgen-ray irradiation in massive doses.

[ED. NOTE.—The most important factor determining postoperative results in cases of renal cancer is the histologic type of the tumor. Foulds,[25] in a study of 295 renal tumors, at the Mayo Clinic, found that cystologically and histologically they grouped themselves according to Ewing's [26] classification, and that this classification was a distinct help in predicting the postoperative results.

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24. Dresser, Richard: Metastatic Manifestations of Hypernephroma in Bone, Am. J. Roentgenol. **13**:342, 1925.

25. Foulds, G. S.: Carcinoma of the Kidney in the Adult, Med. Bull. St. Michael's Hosp. (Toronto) **5**:4, 1924.

26. Ewing, James: Neoplastic Diseases, Philadelphia, W. B. Saunders Company, 1922.

As a basis for prognosis it was found that in the case of malignant cystadenoma the proportion of living to dead was 2:1; in papillary carcinoma with clear cells, 1:1; in adenocarcinoma with granular cells, 1:3, and in alveolar carcinoma, 1:7.

Extension of carcinoma into the renal vein has long been observed and metastasis to the lung, bones and liver is usually recognized as being brought about in this manner. Such involvement of the renal vein begins in the small vessels, as was shown in a case reported by Keyser and Foulds.[27] That venous involvement is of grave import is shown by the fact that, of forty-five patients whose renal veins were grossly involved with tumor, nine died in the hospital, twenty-two died subsequently, five remained untraced, and only nine are known to be alive. However, certain patients survive for a long time. Albrecht [28] discusses two patients, in whom neoplasm had invaded the renal veins, who were alive and well four and a half years, and twelve years, respectively, after operation. Hyman [29] mentions two patients alive and well three and a half years, and four and a half years after nephrectomy. In the Mayo Clinic series, four remained well for six years, one for seven, one for eight, one for twelve years, and one for fourteen years after operation. Judd and Scholl [30] reported an unusual example of a fatal embolus arising from adenocarcinoma of the kidney which involved the renal vein and the vena cava.

In studying the gross pathology, two factors stand out: the size and site of the tumor. The size of the tumor bears a distinct relationship to the postoperative results. This is also apparent in the high mortality among patients with tumors that had caused such extensive destruction by their growth that their original site could not be determined. Large tumors are not only more difficult to remove completely, but also show a greater tendency to perirenal and pelvic involvement. If the tumor is situated in the median portion of the kidney there is early evidence of its presence, and it is discovered while relatively small. There is a larger percentage of living patients in this group than in the group of patients with polar tumors.

Involvement of the renal pelvis or extension through the renal capsule indicates that the disease is well advanced and that the prognosis is bad. Mere encroachment on the renal pelvis without actual involvement does not affect the course of the disease adversely.]

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27. Keyser, L. D., and Foulds, G. S.: The Extension of Hypernephroma by Way of the Renal Vein, J. Urol. **7**:463, 1922.

28. Albrecht, Paul: Beiträge zur Klinik und pathologischen Anatomie der malignen Hypernephrome, Arch. f. klin. Chir. **77**:1073, 1905.

29. Hyman, A.: Tumors of the Kidney, Surg. Gynec. Obst. **32**:216, 1921.

30. Judd, E. S., and Scholl, A. J.: Thrombosis and Embolism Resulting from Renal Tumors, J. A. M. A. **82**:75 (Jan. 12) 1924.

Albrecht found metastatic involvement in eight of fourteen carefully traced patients, and noted pulmonary metastasis in all cases in which the disease was advanced. The average postoperative length of life in twenty-one patients, of the Mayo Clinic series, who died from metastasis was less than three years.

Cases are recorded in the literature of patients who remained in perfect health for several years and then died from metastasis. Among the outstanding cases are those of Albrecht and Clairmont, in which the patients lived for seven and ten years, respectively, after operation, and died later from metastasis.

Broster [31] reports the case of a patient who remained well for nine years after nephrectomy by Thompson-Walker, and then suffered a spontaneous fracture of the femur, the result of secondary tumor. Cases like these make one doubt reports of cure in cases of hypernephroma. Certainly the three or five year series usually allowed in other types of malignancy is inadequate in renal tumors.

Tumor of the Renal Capsule.—Haslinger [32] states that the most common renal tumors are hypernephroma, carcinoma and sarcoma. Tumors of the capsule and perirenal fat are noteworthy for their infrequency. They are rarely diagnosed preoperatively. In spite of the progress of urologic diagnosis, it is often impossible to ascertain whether a tumor is in the parenchyma or in the capsule. Infiltration to the adjacent organs confuses the diagnosis and makes excision extremely difficult.

Haslinger reports a case of a patient, aged 53, with a tumor in the region of the right kidney. She complained of gastric pressure, nausea, vomiting and belching. Cystoscopy and pyelography showed kinking of the right ureter with the kidney displaced downward and calcareous deposits along its outline. Exploratory operation revealed a tumor around the kidney, involving the peritoneum and ascending colon. Death occurred tweny-four days after operation. At necropsy a tumor, 25 cm. long, 12 cm. wide and 7 cm. thick, was found. Pathologically, it was of a mixed type, showing mainly a fibrolipoma with lipoblasts; in another section there was a vascularized polymorphocellular sarcoma. Throughout the tumor were deposits of bone.

In discussing these cases, Haslinger states that tumors of the hilum of the kidney must be differentiated into connective tissue tumors of the renal capsule and those of the perirenal fat layer. The former are the more uncommon. Pathologically, they are either pure lipomas, fibromas or mixed tumors undergoing malignant degeneration. Liebermann, in 1921, reviewed cases of 165 such tumors and found 46 per cent lipomas,

31. Broster, L. R.: A Case of Secondary Hypernephroma in the Femur with Spontaneous Fracture, Brit. J. Surg. **11**:287, 1923-1924.

32. Haslinger, Kolman: Zur Kasuistik der Nierenkapseltumoren, Ztschr. f. urol. Chir. **20**:89, 1926.

20 per cent fibrolipomas, 10 per cent myolipomas, 10 per cent fibromyolipomas and 14 per cent sarcomas. Alexander considered heredity, congenital disposition, peripheral nervous disturbances and diseases of the thyroid and hypophysis as possible factors in the etiology. Birsch-Hirschfeld classified them as embryonic adenosarcomas or sarcomatous glandular swellings. He believes that they originate in a part of the wolffian body which has continued to develop after birth. These tumors have also been designated as blastomas because often many connective tissue elements are present. Bone has often been found. Haslinger believes that these tumors may possibly be due to pressure on the renal artery or to bleeding in the renal capsule followed by organization. Muscle tissue has also been found. Because of the presence of the many and varied tissues, some observers have considered the tumors embryonic in type. Many are characteristic because of their large growth, ranging in weight sometimes from 30 to 60 pounds (13.6 to 27.2 Kg.). There is a marked tendency to recur. The operative mortality is high, but the chief cause of death is from recurrence. Haslinger advises a transperitoneal approach and resection of all the perirenal fat. If possible, the tumor should be removed and the kidney left, if it is in good condition.

Tumor of the Renal Pelvis.—Haslinger [33] notes that papillomatous tumors of the renal pelvis are rare, in spite of the numerous publications concerning them that have appeared in recent years. In sixteen years only two cases were found in his clinic, although during the same time 306 (0.65 per cent) kidneys had been operated on. The etiology is not clear, but hereditary disposition of the mucous membrane toward tumor formation, chronic irritation through pyelitis, calculi, chemical irritation and other causes are cited as possibilities. The literature shows that 50 per cent of the tumors undergo malignant degeneration and spread to the ureter and bladder. Diagnosis offers many difficulties. Because of the tendency of the tumors to spread and become malignant, the only treatment is nephro-ureterectomy. Haslinger reports two cases, in one of which there was a double ureter.

Interrenal Tumor.—Gordon and Feldman [34] described an interesting retroperitoneal tumor. The situation is difficult to diagnose accurately, unless urinary disturbances are associated. The possible conditions to be considered are the retroperitoneal lymphosarcomas, lipomas, fibromas and various tumor-like disturbances of development connected with the suprarenals, kidney or retroperitoneal cysts. The case of a woman, aged 60, is reported, who had intermittent pain and swelling in the region of the left kidney for four years. The pain gradually became

33. Haslinger, Kolman: Die Zottengeschwülste des Nierenbeckens, Ztschr. f. urol. Chir. **20**:77, 1926.

34. Gordon, W. H., and Feldman, M. S.: An Unusual Abdominal Neoplasm: Interrenal Rhabdomyoma, Ann. Clin. Med. **3**:706, 1924-1925.

more severe and was associated with constipation and bloody stools. Operation revealed an extensive carcinoma which apparently involved the pancreas. Roentgen-ray treatment was instituted, but did not relieve her. Later, on cystoscopic examination, a provisional diagnosis of tumor of the left kidney was made. Dr. Hugh Cabot operated and found a large inoperable tumor resembling a retroperitoneal sarcoma, the source of which he was unable to determine. Further roentgen-ray treatment was given and finally to control the pain a cordotomy was performed. The patient continued to fail and died several months later.

At necropsy the tumor appeared to have originated at the juncture of the celiac axis and the aorta. It involved the renal pelvis, left suprarenal, pancreas, aorta and adjacent tissues. When sectioned it resembled an ordinary myoma of the uterus. The diagnosis of various pathologists to whom tissue was submitted are substantially as follows: (1) leiomyosarcoma arising from the aortic wall, with low grade of malignancy (P. F. Morse); (2) congenital interrenal rhabdomyoma, cellular and atypical in areas, to be called a rhabdomyosarcoma, of local malignancy only and arising primarily in a disturbance of development of the myotome (A. S. Warthin); (3) leiomyosarcoma (malignant leiomyoma) (B. Lucke), and (4) leiomyosarcoma (J. Ewing). In the final discussion the tumor was called a rhabdomyoma.

Clinically, rhabdomyomas are most often found in the genito-urinary tract. They usually grow slowly, but may undergo malignant changes and grow rapidly. In the differential diagnosis of retroperitoneal tumors the possibility of congenital disturbances of development in the form of interrenal teratomas genetically related to those of the kidney must be considered.

Renal Cyst.—Begg [35] asserts that solitary hemorrhagic cysts of the kidney are rare, only about twelve cases being reported. These cysts are of the nature of partial hematonephrosis when the source of the bleeding remains active for a long time. In some instances the cyst may arise from an angioma of the renal parenchyma. Begg reports a case in which the lower pole of the kidney is entirely occupied by a cystic tumor 11 cm. in diameter. The wall of the cyst is definitely fibrous, and varies in thickness between 1 and 2.5 mm. On incising the tumor, 250 cc. of dark fluid blood and tarry clot escaped. The internal lining of the cyst is smooth and glistening, except where masses of fibrin and clot are adherent. No dilated veins and no focus of bleeding are apparent in the wall of the cyst. The upper major calix of the renal pelvis is normal, the lower is absent. A slight connection exists between the upper part of the cyst and the pelvis, through which a

35. Begg, R. C.: Solitary Haemorrhagic Cysts of the Kidney; with a Report of a Case Originating in a Cavernous Haemangioma Brit. J. Surg. **13**:649, 1926.

bristle can be passed. At two points bosses project externally. At the upper part the cyst is separated from the remainder of the kidney by its laminated fibrous wall, and the part of the kidney immediately adjacent to this appears to be pale and compressed. The internal measurements of the cyst are 9.2 cm. from above down, and 6.8 cm. in the other two diameters. The whole was covered by the fibrous capsule of the kidney, which passed without interruption into the capsule of the sound part of the organ.

Extrarenal Hypernephroma.—Tyson [36] reports a case of hypernephroma of the gallbladder in a woman, aged 63. The gallbladder was removed, and the patient recovered from the operation. On section the gallbladder was a mass of growth. The histologic characters of the tumor were identical with those described as being typical of hypernephroma by Grawitz in 1883. No portion of gallbladder could be identified in the sections. But at one side there was a small portion of liver. The clear cells with distinct walls supported by a fibrous stroma could not be confused with those of any other neoplasm. Piney, who examined the tumor, said that the present tendency is to regard renal hypernephroma as being derived from altered renal cells, and there can be no doubt that true suprarenal rests in this organ are far from common, although the theory that hypernephromas grow from such structures would presuppose their comparatively frequent presence.

Suprarenal rests are extremely common in certain situations, for example, along the spermatic cord, in the broad ligament and on the under surface of the liver, but no record is available of such a structure in the wall of the gallbladder. Borst is still strongly of the opinion that the majority, if not all, hypernephromas are of suprarenal origin, and there is much to support this view; if it is accepted, the explanation of the genesis of the present tumor would not present insuperable difficulties. The neoplastic growth, either of suprarenal rest in the liver near the gallbladder or in the wall of the gallbladder, would well account for its occurrence.

Pyelonephritis.—Caulk [37] reviewed 2,100 cases of renal infection; 1,191 occurred in adults and 909 in children. The relative frequency in male and female seems dependent on the period of life. In children, girls predominate, 3:1. In this series there were 684 girls and 225 boys; in adults the proportion is almost 2:1; 755 were women and 436 were men. In 102 cases renal infection complicated pregnancy. With this contributing element eliminated, the incidence is not strikingly different; about 33 per cent in favor of the female. In the latter period

36. Tyson, Wilson: Hypernephroma of Gall-Bladder: Cholecystectomy, Brit. J. Surg. **13**:757, 1926.

37. Caulk, J. R.: Pyelonephritis: Its Incidence, Engendering Elements and Impelling Influences, J. Urol. **16**:117, 1926.

of life, between the ages of 50 and 80, when renal infections resulting from obstructions of the lower urinary tract are so frequent in men, the proportion in men and women is more nearly equal, being 163 : 201.

The most important feature, not only in the production but in the perpetuation of renal infection, is stasis. It may be the result of pre-existing pathologic processes within the urinary tract, or secondary to some extrinsic influence, particularly to pressure resulting from morbid processes in some of the other organs or tissues, or it may be self-engendered or automatic and secondary to the infection from the kidney itself. The latter type is Caulk's impression of the fundamental feature in the foreground of so-called acute pyelonephritis, which usually disappears spontaneously, but in many instances leaves its scar.

Opinion has varied relative to stasis resulting from preëxisting obstruction. If one should accept the work of Biedl and Kraus, Lamierre and Abrami, Mayer, Heyn and others, that a healthy kidney excretes bacteria, it would be perfectly easy to explain these infections as "filth in a pool," or the contamination of a stagnant pond, but the work of Pernice, Scagliose, Sherrington, Dyke, and particularly that of Helmholz, has shown definitely that bacteria are not excreted through a kidney unless the integrity of its secreting surface has been broken. Therefore, it must be a question of pressure and the effect exerted on the circulatory bed. Whatever the cause, the effect when once produced should be remedied as promptly as possible to protect against back pressure; whether this is through the tubular system, lymphatic, or the venous channels, as Hinman recently described, the secretory surface should be protected from further invasion.

Lévy-Dreyfus [38] reports an unusual case of bilateral pyelonephritis complicated by severe hematuria. The hematuria, which was profuse, was the first symptom and had started three days previously. During the same period there had been dysuria and frequency, which disappeared after forty-eight hours. The patient had diabetes, obstinate chronic constipation and a cardiac lesion. Physical examination revealed a tender right kidney. Cystoscopic examination of the bladder gave negative results. Both ureters were catheterized, following which severe hematuria and pain on the right side again occurred several hours later. Roentgenograms of the kidneys were negative. Eight days later, after a second ureteral catheterization, a large amount of blood was found in the urine from both kidneys, as well as pus, colon bacilli and staphylococci. The capacity of each pelvis was 9 cc. A seventy minute phenolsulphonphthalein test showed a return of 22 per cent on the right and 21 per cent on the left. A diagnosis of bilateral subacute pyelo-

38. Lévy-Dreyfus, R.: Pyélonéphrite à forme hématurique chez une diabétique. Infection urineuse aiguë consecutive au cathétérisme uréteral, Strasbourg méd. **83**:351, 1925; abstr., Ztschr. f. urol. Chir. **19**:440, 1926.

nephritis was made. Several hours after the ureteral catheterization, the patient had a chill, increased temperature, thready pulse, profuse hematuria and frequency. She was given caffeine and camphor, and 1 Gm. methenamine intravenously. The retention catheter was left in place for five days, during which time the urine became normal. The patient was placed on a milk and vegetable diet for five weeks, and the bladder was irrigated frequently. She recovered, and the urine was free from pus and bacteria.

[ED. NOTE.—This type of urinary infection is rare, but it has previously been described by Marion. The heavy renal bleeding may readily complicate the diagnosis; the high temperature is unusual and may be explained by the presence of the diabetes. The important points in the treatment of the case are the insertion of the retention catheter and frequent irrigations of the bladder.]

Dudgeon,[39] in a symposium on renal infections at the Royal Society of Medicine, classified the types of infection into: (1) infections due to a special group of hemolytic bacilli, (2) infection due to *Bacillus coli*, (3) *Bacillus proteus* and (4) *Staphylococcus albus*.

The great differences between the special hemolytic bacillus infection and those due to *Bacillus coli* were that they ran a more acute course as a rule, and were of longer duration, that complete recovery usually occurred and the urine became free from the infective organism, and that there was hypersensitiveness to specific vaccines.

Colon bacilli infecting the urinary tract may be grouped into hemolytic and nonhemolytic strains. The hemolytic group accounted for about 70 per cent of cases in men and about 30 per cent in women, although the percentage was higher in women suffering from acute fever. With the nonhemolytic group the percentages among men and women were reversed. Rabbits were readily immunized by the hemolytic group, but often with great difficulty by the nonhemolytic.

Although from inexperience *Bacillus proteus* had been regarded as nonpathogenic to man, it is well to realize that it may give rise to acute infections, and the bacillus can then be recovered from the blood stream. The temperature in some proteus infections reaches a high level. The urine is alkaline, contains mucus and pus and often masses of triple phosphate with the mucus. Vaccine treatment has been found to be of definite value when the acute stage is over.

The presence of *Staphylococcus albus* in large numbers in the urine, together with pus, was, in the author's experience, invariably associated with the presence of a calculus.

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39. Dudgeon, L. S.; Lepper, Elizabeth, and Thomson-Walker, J. Discussion on Bacterial Infections of the Urinary Tract, Proc. Roy. Soc. Med. **18**:43, 1925.

Lepper,[39] after reviewing the literature, concluded that in spite of apparently contradictory statements, the following facts had been established: (1) It is comparatively easy to produce lesions in a kidney by injections of organisms either into the blood stream or into the ureter, provided some obstruction of the ureter is produced at that time, and (2) inflammatory changes of the substance of the kidney or its pelvis can be produced by the intravenous injection of bacilli alone, without the presence of obstruction to the outflow of the urine; the occurrence of such lesions is, however, uncertain, as is also the degree of severity and their localization.

Experiments were carried out by Lepper to produce an early slight lesion in order to determine why obstruction to the outflow of urine is so important. She found that in the experimental production of lesions in the kidney, obstruction of the ureter is important in bringing about dilatation of the pelvis and pressure on the veins, which may result in extravasation of infected blood into the substance of the kidneys, and subsequently diffuse inflammatory changes throughout the kidney. Intravenous injection alone, however, acts by producing embolism of small arteries, especially those supplying the papilla; the lesions are localized, and much less severe than those produced by the extravasation of infected blood into the tissues, such as occurs after obstruction of the ureter.

Thomson-Walker[39] divides urinary infection into two groups: (1) infection in a urinary tract already the seat of disease, such as stricture, enlarged prostate, growths in the bladder or stone, and (2) infection in a previously healthy urinary tract. In the present discussion, he deals only with the latter. He describes fully the symptoms and course of acute infections. The more obscure clinical cases in which the symptoms do not present themselves so clearly include those in which high temperature may be the only symptom, and in which only examination of the urine will reveal the nature of the disease. This is more often seen in children. In other cases, pain alone may be present or may be the most prominent symptom. The aching pain of pyelitis may be mistaken for appendicitis. Hematuria as an initial symptom may prove puzzling. There is also a group of cases, fortunately a small one, in which the infection is cortical, and in which the urine remains sterile.

There are three common varieties of chronic renal infection: (1) recurrent pyelitis and cystitis, (2) chronic cystitis with quiescent pyelitis and (3) bacilluria with toxemia. The infecting organism is commonly *Bacillus coli,* which is normally present in the bowel. Thomson-Walker has noted the frequent association of handling the bowel in the course of abdominal surgery and subsequent pyelitis. He therefore recommends the administration of methenamine prior to

abdominal operations. In discussing treatment he reviews the use of alkalies, diuretics and urinary antiseptics. He cautions against the use of hexylresorcinol in cases in which chronic nephritis is associated. His remarks on the use of intravenous injections of drugs are disparaging. He approves of renal lavage in the chronic cases.

Feirer, Meader and Leonard [40] made a study of the drugfast character of organisms. They used cultures as follows: the Hopkins strain of *Bacillus typhosus;* a strain of *Bacillus coli* isolated from the stool of a typhoid carrier who had been taking hexylresorcinol for one year; a strain of *Bacillus coli* isolated from the stool of a normal adult; a strain of *Bacillus lactis aerogenes* isolated from the urine of a patient who had been taking hexylresorcinol for more than one year, and a strain of *Bacillus coli* isolated from the urine of a patient who had not taken any drug.

They investigated the development of the drugfast character in these strains to: silver nitrate, mercurochrome 220-soluble, formaldehyde (to represent methenamine), acriflavine, hexylresorcinol and phenol.

It is clear that the resistance of certain organisms to the bacteriostatic influence of the drugs ordinarily employed in the treatment of urinary infections may be raised to a high degree, that this resistance is highly specific and that in acquiring it the strain may become much more sensitive to the action of certain other germicides. It was hoped that this investigation would result in an exact and explicit method of drug rotation so that the treatment of all these infections might be begun with a definite drug for the purpose of enhancing greatly the susceptibility of the offending organism to the action of another. While these experiments point definitely to principles which may have an important clinical bearing, the few cultures examined vary too widely in their reactions to these germicides to admit of sweeping conclusions.

The authors found that *Bacillus coli* and *Bacillus lactis aerogenes* may develop enormous resistance to the action of silver nitrate and mercurochrome-220 soluble when exposed in the test tube to concentrations of these germicides permitting growth. Under the same conditions these organisms may become from five to fourteen times more resistant to the bacteriostatic action of formaldehyde and acriflavine, but develop only a relatively slight tolerance to hexylresorcinol and phenol.

The drugfast character is highly specific. None of the thirty drugfast substrains showed increased tolerance to any of the germicides ordinarily employed in the treatment of urinary infections other than the particular one to which it had been exposed.

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40. Feirer, W. A.; Meader, P. D., and Leonard, V.: Development of the Drug Fast Character in Vitro and Its Bearing upon Drug Rotation in the Management of Chronic Urinary Infections, J. Urol. **16**:97, 1926.

The acquirement by bacteria of a specific drugfast character may be accompanied by a greatly increased sensitiveness to the action of other germicides, but this increased sensitiveness bears no relationship to the degree of drugfastness acquired. A substrain which has acquired great resistance to the action of a derivative of one of the heavy metals (mercurochrome) may show no marked increase in sensitiveness to other germicides, while the same cultures exposed to the action of a drug which does not lend itself to the development of more than a slight degree of the drugfast character (hexylresorcinol) may become much more sensitive to the action of other germicides.

While cultures exposed to the action of one germicide (hexylresorcinol) may develop substrains of much greater sensitiveness to the action of another (formaldehyde), the substrains of the same cultures developed by exposure to the action of the latter germicide may show no increased sensitiveness to the former. The authors suggest that the results of these experiments indicate a logical plan of drug rotation in the treatment of chronic urinary infections.

If treatment has not been given, hexylresorcinol should be administered by mouth for a period of from thirty to sixty days. Large doses should then be substituted, and silver nitrate solutions employed locally. Throughout this treatment the fluid intake should not be increased. If silver nitrate has been used persistently, hexylresorcinol or acriflavine should be administered by mouth, and acriflavine should be employed locally. If mercurochrome has been used persistently, the offending organism has probably developed an increased resistance to mercury. Hexylresorcinol or acriflavine should be administered by mouth, to be followed after from thirty to sixty days by methenamine in large doses and silver nitrate locally. If methenamine has been used persistently, the organism may have developed increased sensitiveness to silver nitrate, and this should be tried locally. If no improvement results, the rotation should be as indicated in an untreated patient.

If acriflavine has been used persistently, silver nitrate should be employed locally and methenamine or hexylresorcinol administered by mouth. If hexylresorcinol has been used persistently, large doses of methenamine should be substituted, together with silver nitrate solutions locally. If no improvement results, acriflavine should be administered by mouth for from thirty to sixty days, to be followed by large doses of methenamine and silver nitrate locally.

If these various rotations prove to be unsuccessful, the management should be that arranged for an untreated patient. It should be recalled in this connection that the highest percentage of cures ever obtained in a series of chronic urinary infections was reported by Henline, of the New York Hospital, following the simultaneous use of hexylresorcinol by mouth and acriflavine locally. There may well be some particular

advantage in this method, although it does not appear to be related to the development of the drugfast character.

Any change from one drug to another should be sudden and complete, and there should be no interval of suspended treatment between the two. The drugfast character developed in the test tube is lost, to some extent at least, after a few days' cultivation of the organism in a drug-free environment, and its enhanced susceptibility to the action of other germicides may presumably become lessened in like degree under these circumstances.

Perinephritic Abscess.—Pugh [41] reports two cases of perinephritic abscess; one in a girl aged 5, the other in a boy, aged 8. Both were successfully operated on under local anesthesia. Pugh concludes that perinephritic abscess formation, particularly that due to metastasis, is more common than is generally supposed. The history of infection and pain in the costovertebral angle in children suggests the condition. All doubtful cases should be studied thoroughly from a urologic standpoint and an exploratory operation performed; it can and should be performed under local anesthesia.

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41. Pugh, W. S.: Perinephritic Abscess in Children, Urol. & Cutan. Rev. **29**:387, 1925.

(To be continued)